Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US05/006627

International filing date: 24 February 2005 (24.02.2005)

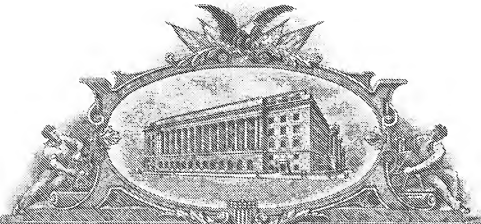
Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/548,154
Filing date: 25 February 2004 (25.02.2004)

Date of receipt at the International Bureau: 18 April 2005 (18.04.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)

World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse



1503238

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

March 31, 2005

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: ***60/548,154***
FILING DATE: ***February 25, 2004***
RELATED PCT APPLICATION NUMBER: ***PCT/US05/06627***

Certified by

Jon W. Dudas

Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office

PTO/SB/16 (01-04)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. EL 997866461 US

INVENTOR(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Lin	Zhi	San Diego, California

Additional inventors are being named on the 1 *separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

GLUCOCORTICOID RECEPTOR MODULATOR COMPOUNDS AND METHODS

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

☑ Customer Number:

36183

PATENT TRADEMARK OFFICE

OR

☐ Firm or Individual Name					
Address					
Address					
City		State		Zip	
Country		Telephone		Fax	

ENCLOSED APPLICATION PARTS *(check all that apply)*

☑ Specification *Number of Pages* 191

☐ CD(s), Number

☐ Drawing(s) *Number of Sheets*

☑ Other (specify) cvr sheet & postcard

☑ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check or money order is enclosed to cover the filing fees.

☐ The Director is herby authorized to charge filing fees or credit any overpayment to Deposit Account Number:

☐ Payment by credit card. Form PTO-2038 is attached.

FILING FEE Amount ($)

The Invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☑ No.

☐ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

SIGNATURE

Date February 25, 2004

REGISTRATION NO. 47,224 *(if appropriate)*

Docket Number: 45026.00152.PRV

TYPED or PRINTED NAME Jane K. Babin, Ph.D., Esq.

TELEPHONE (858) 720-2677

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

PROVISIONAL APPLICATION COVER SHEET
Additional Page

PTO/SB/16 (08-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Docket Number 45026.00152.PRV

INVENTOR(S)/APPLICANT(S)

Given Name (first and middle [if any])	Family or Surname	Residence (City and either State or Foreign Country)
Robert J. Dean	Ardecky Phillips	Encinitas, California San Marcos, California
John S. Donald S.	Tyhonas Karanewski	San Diego, California Escondido, California

Number 2 of 2

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

PATENT
45026.00152.PRV

PROVISIONAL APPLICATION UNDER 37 CFR § 1.53(C)

TITLE: **GLUCOCORTICOID RECEPTOR MODULATOR COMPOUNDS AND METHODS**

APPLICANTS: Lin Zhi
Robert J. Ardecky
Dean Phillips
John S. Tyhonas
Donald S. Karanewski

Correspondence Enclosed:

Provisional Application Cover Sheet (1 pg); Provisional Application for Patent Cover Sheet (PTO/SB/16 – 2 pgs); Specification (168 pgs); Claims (22 pgs); Abstract (1 pg); and Return Postcard.

CERTIFICATE OF MAILING BY EXPRESS MAIL

Express Mail Label No. EL 997866461 US

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail Post Office to Addressee with sufficient postage on the date indicated below and is addressed to: Mail Stop Provisional Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date of Deposit : February 25, 2004

Signature Janice Crisp

Typed Name of Person Signing: Janice Crisp

GLUCOCORTICOID RECEPTOR MODULATOR COMPOUNDS AND METHODS

Background of the Invention

Field of the Invention

[001] This invention relates to compounds that bind to glucocorticoid receptors and/or modulate activity of glucocorticoid receptors, and to methods for making and using such compounds.

Background

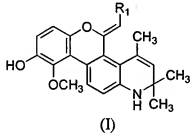
[002] Certain intracellular receptors (IRs) have been shown to regulate transcription of certain genes. *See e.g.*, R. M. Evans, Science, *240*, 889 (1988). Certain of such IRs are steroid receptors, such as glucocorticoid receptors, androgen receptors, estrogen receptors, mineralocorticoid receptors, and progesterone receptors. Gene regulation by such receptors typically involves binding of an IR by a ligand.

[003] In certain instances, a ligand binds to an IR, forming a receptor/ligand complex. Such a receptor/ligand complex may then translocate to the nucleus of a cell, where it may bind to the DNA of one or more gene regulatory regions. Once bound to the DNA of a particular gene regulatory region, a receptor/ligand complex may modulate the production of the protein encoded by that particular gene. In certain instances, a glucocorticoid receptor/ligand complex regulates expression of certain

proteins. In certain instances, a glucocorticoid receptor/ligand complex may interact directly with the DNA of a particular gene regulatory region. In certain instances, a glucocorticoid receptor/ligand complex may interact with other transcription factors, such as activator protein-1 (AP-1) or nuclear factor κB (NFκB). In certain instances, such interactions result in modulation of transcriptional activation.

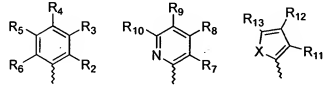
Summary of the Invention

[004] In certain embodiments, the invention provides compounds of Formula I:



(I)

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, wherein R_1 is selected from Formula II, III, and IV:



(II) (III) (IV)

wherein:

R_2 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-CONR_{14}R_{15}$, $-OR_{16}$, $-SR_{16}$, $-SO_2NR_{14}R_{15}$, and an optionally substituted aryl,

R_3 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-OR_{16}$, $-SR_{16}$ and an optionally substituted aryl, and

R_4 is selected from hydrogen, F, Cl, Br, CN, $-OR_{16}$, a ring, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_2 and R_3 together form an optionally substituted 5-6 member ring and R_4 is selected from hydrogen, F, Cl, Br, CN, $-OR_{16}$, a ring, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_3 and R_4 together form an optionally substituted 4-6 member ring and R_2 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-CONR_{14}R_{15}$, $-OR_{16}$, $-SR_{16}$, $-SO_2NR_{14}R_{15}$, and an optionally substituted aryl;

R_5 is selected from hydrogen, F, Cl, Br, optionally substituted C_1-C_4 alkyl, and OCH_3;

R_6 is selected from hydrogen and F;

R_7 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl,

R_8 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -OR_{16}, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, and

R_9 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_7 and R_8 together form an optionally substituted 5-6 member ring and R_9 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, or

R_8 and R_9 together form an optionally substituted 4-6 member ring and R_7 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl;

R_{10} is selected from hydrogen, F, Cl, CH_3, and OCH_3;

R_{11} is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl,

R_{12} is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -OR_{16}, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, and

R_{13} is selected from hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_{11} and R_{12} together form an optionally substituted 5-6 member ring and R_{13} is selected from hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_{12} and R_{13} together form an optionally substituted 4-6 member ring and R_{11}, is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl;

R_{14} and R_{15} are each independently selected from hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_{14} and R_{15} together form an optionally substituted 4-7 member ring;

R_{16} is selected from hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, and an optionally substituted aryl;

X is selected from O, S, and NR_{17}; and

R_{17} is selected from hydrogen and an optionally substituted C_1-C_4 alkyl;

wherein

at least one position selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen;

at least one position selected from R_7, R_8, R_9, and R_{10} is not hydrogen;

if R_4 is F, then at least one position selected from R_2, R_3, R_5 and R_6 is not hydrogen;

if R_3 is F, then at least one position selected from R_2, R_4, R_5, and R_6 is not hydrogen; and

if any two positions selected from R_2, R_3, R_4, R_5, and R_6 are both F, then at least one of the other three positions selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen.

[005] In certain embodiments, the invention provides methods for modulating at least one activity of a glucocorticoid receptor. Certain of such methods comprise contacting a glucocorticoid receptor with one or more compounds of the present

invention.

[006] In certain embodiments, the invention provides a method for identifying a compound that is capable of modulating activity of a glucocorticoid receptor, comprising: a) contacting a cell expressing the glucocorticoid receptor with a compound of the present invention; and b) monitoring an effect of the compound upon the cell. In certain of such embodiments, the compound is derived from a quinoline. In certain embodiments, the compound is a 6-arylquinoline.

[007] In certain embodiments, the invention provides methods for treating a patient comprising administering to the patient a compound of the present invention.

[008] In certain embodiments, the invention provides a method of treating a condition including, but not limited to, inflammation (including, but not limited to, rheumatoid arthritis, asthma (acute and/or chronic), lupus, osteoarthritis, rhinosinusitis, inflammatory bowel disease, polyarteritis nodosa, Wegener's granulomatosis, giant cell arteritis, allergic rhinitis, urticaria, hereditary angioedema, chronic obstructive pulmonary disease, tendonitis, bursitis, autoimmune chronic active hepatitis, cirrhosis), transplant rejection, psoriasis, dermatitus, autoimmune disorders, malignancies (*e.g.*, leukemia, myelomas, lymphomas), acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, granulomatous disease, immune proliferation/apotosis, HPA axis suppression and regulation, hypercortisolemia, modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hyperglycemia, cerebral edema, thrombocytopenia, Little's syndrome, Addison's disease,

cystic fibrosis, myasthenia gravis, autoimmune hemolytic anemia, uveitis, pemphigus vulgaris, multiple sclerosis, nasal polyps, sepsis, infections (*e.g.,* bacterial, viral, rickettsial, parasitic), type II diabetes, obesity, metabolic syndrome, depression, schizophrenia, mood disorders, Cushing's syndrome, anxiety, sleep disorders, memory and learning enhancement, or glucocorticoid-induced glaucoma.

[009] In certain embodiments, the invention provides a pharmaceutical agent comprising: i) a physiologically acceptable carrier, diluent, or excipient, or a combination thereof; and ii) one or more compounds of the present invention.

Detailed Description

[010] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention claimed. In this application, the use of the singular includes the plural unless specifically stated otherwise. In this application, the use of "or" means "and/or" unless stated otherwise. Furthermore, use of the term "including" as well as other forms, such as "includes," and "included," is not limiting.

[011] The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. All documents, or portions of documents, cited in the application including, but not limited to, patents, patent applications, articles, books, manuals, and treatises are hereby expressly incorporated by reference in their entirety for any purpose.

Definitions

[012] Unless specific definitions are provided, the nomenclatures utilized in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those known in the art. Standard techniques may be used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients. Standard techniques may be used for recombinant DNA, oligonucleotide synthesis, and tissue culture and transformation (*e.g.*, electroporation, lipofection). Reactions and purification techniques may be performed *e.g.*, using kits according to manufacturer's specifications or as commonly accomplished in the art or as described herein. The foregoing techniques and procedures may be generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification. *See e.g.*, Sambrook et al. Molecular Cloning: A Laboratory Manual (2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)), which is incorporated herein by reference for any purpose.

[013] As used herein, the following terms are defined with the following meanings, unless explicitly stated otherwise.

[014] The term "selective binding compound" refers to a compound that selectively binds to any portion of one or more target receptors.

[015] The term "selective glucocorticoid receptor binding compound" refers to

a compound that selectively binds to any portion of a glucocorticoid receptor.

[016] The term "selectively binds" refers to the ability of a selective binding compound to bind to a target receptor with greater affinity than it binds to a non-target receptor. In certain embodiments, specific binding refers to binding to a target with an affinity that is at least 10, 50, 100, 250, 500, or 1000 times greater than the affinity for a non-target.

[017] The term "target receptor" refers to a molecule or a portion of a receptor capable of being bound by a selective binding compound. In certain embodiments, a target receptor is a glucocorticoid receptor.

[018] The term "modulator" refers to a compound that alters an activity of a molecule. For example, a modulator may cause an increase or decrease in the magnitude of a certain activity of a molecule compared to the magnitude of the activity in the absence of the modulator. In certain embodiments, a modulator is an inhibitor, which decreases the magnitude of one or more activities of a molecule. In certain embodiments, an inhibitor completely prevents one or more activities of a molecule. In certain embodiments, a modulator is an activator, which increases the magnitude of at least one activity of a molecule. In certain embodiments the presence of a modulator results in an activity that does not occur in the absence of the modulator.

[019] The term "selective modulator" refers to a compound that selectively modulates a target activity.

[020] The term "selective glucocorticoid receptor modulator" refers to a

compound that selectively modulates at least one activity associated with a glucocorticoid receptor.

[021] The term "selectively modulates" refers to the ability of a selective modulator to modulate a target activity to a greater extent than it modulates a non-target activity.

[022] The term "target activity" refers to a biological activity capable of being modulated by a selective modulator. Certain exemplary target activities include, but are not limited to, binding affinity, signal transduction, enzymatic activity, tumor growth, and inflammation or inflammation-related processes.

[023] The term "receptor mediated activity" refers any biological activity that results, either directly or indirectly, from binding of a ligand to a receptor.

[024] The term "agonist" refers to a compound, the presence of which results in a biological activity of a receptor that is the same as the biological activity resulting from the presence of a naturally occurring ligand for the receptor.

[025] The term "partial agonist" refers to a compound the presence of which results in a biological activity of a receptor that is of the same type as that resulting from the presence of a naturally occurring ligand for the receptor, but of a lower magnitude.

[026] The term "antagonist" refers to a compound, the presence of which results in a decrease in the magnitude of a biological activity of a receptor. In certain embodiments, the presence of an antagonist results in complete inhibition of a biological activity of a receptor.

[027] The term "alkyl" refers to an aliphatic hydrocarbon group. An alkyl group may be a "saturated alkyl," which means that it does not contain any alkene or alkyne groups. An alkyl group may be an "unsaturated alkyl," which means that it comprises at least one alkene or alkyne group. An alkyl, whether saturated or unsaturated, may be branched, straight chain, or cyclic.

[028] In certain embodiments, an alkyl comprises 1 to 20 carbon atoms (whenever it appears herein, a numerical range such as "1 to 20" refers to each integer in the given range; *e.g.*, "1 to 20 carbon atoms" means that an alkyl group may comprise only 1 carbon atom, 2 carbon atoms, 3 carbon atoms, *etc.*, up to and including 20 carbon atoms, although the term "alkyl" also includes instances where no numerical range of carbon atoms is designated).

[029] The term "lower alkyl" refers to an alkyl comprising 1 to 5 carbon atoms. The term "medium alkyl" refers to an alkyl comprising 5 to 10 carbon atoms. An alkyl may be designated as "C_1-C_4 alkyl" or similar designations. By way of example only, "C_1-C_4 alkyl" indicates an alkyl having one, two, three, or four carbon atoms, i.e., the alkyl is selected from methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, and t-butyl. Alkyls may be substituted or unsubstituted. Alkyls include, but are not limited to, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tertiary butyl, pentyl, hexyl, ethenyl, propenyl, butenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like, each of which may be optionally substituted.

[030] The term "alkenyl" refers to an alkyl group comprising at least one

carbon-carbon double bond.

[031] The term "alkynyl" refers to an alkyl group comprising at least one carbon-carbon triple bond.

[032] The term "haloalkyl" refers to an alkyl in which at least one hydrogen atom is replaced with a halogen atom. In certain of the embodiments in which two or more hydrogen atom are replaced with halogen atoms, the halogen atoms are all the same as one another. In certain of such embodiments, the halogen atoms are not all the same as one another.

[033] The term "heteroalkyl" refers to a group comprising an alkyl and one or more heteroatoms. Certain heteroalkyls are acylalkyls, in which the one or more heteroatoms are within an alkyl chain. Examples of heteroalkyls include, but are not limited to, $CH_3C(=O)CH_2$-, $CH_3C(=O)CH_2CH_2$-, $CH_3CH_2C(=O)CH_2CH_2$-, $CH_3C(=O)CH_2CH_2CH_2$-, $CH_3OCH_2CH_2$-, CH_3NHCH_2-, and the like.

[034] The term "heterohaloalkyl" refers to a heteroalkyl in which at least one hydrogen atom is replaced with a halogen atom.

[035] The term "carbocycle" refers to a group comprising a covalently closed ring, wherein each of the atoms forming the ring is a carbon atom. Carbocylic rings may be formed by three, four, five, six, seven, eight, nine, or more than nine carbon atoms. Carbocycles may be optionally substituted.

[036] The term "heterocycle" refers to a group comprising a covalently closed ring wherein at least one atom forming the ring is a heteroatom. Heterocyclic rings may

be formed by three, four, five, six, seven, eight, nine, or more than nine atoms. Heterocycles may be optionally substituted. Binding to a heterocycle can be at a heteroatom or via a carbon atom. For example, binding for benzo-fused derivatives, may be via a carbon of the benzenoid ring.

[037] The term "heteroatom" refers to an atom other than carbon or hydrogen. Heteroatoms are typically independently selected from oxygen, sulfur, nitrogen, and phosphorus, but are not limited to those atoms. In embodiments in which two or more heteroatoms are present, the two or more heteroatoms may all be the same as one another, or some or all of the two or more heteroatoms may each be different from the others.

[038] The term "aromatic" refers to a group comprising a covalently closed ring having a delocalized π-electron system. Aromatic rings may be formed by three, four, five, six, seven, eight, nine, or more than nine atoms. Aromatics may be optionally substituted. Examples of aromatic groups include, but are not limited to phenyl, naphthalenyl, phenanthrenyl, anthracenyl, tetralinyl, fluorenyl, indenyl, and indanyl. The term aromatic includes, for example, benzenoid groups, connected via one of the ring-forming carbon atoms, and optionally carrying one or more substituents selected from an aryl, a heteroaryl, a cycloalkyl, a non-aromatic heterocycle, a halo, a hydroxy, an amino, a cyano, a nitro, an alkylamido, an acyl, a C_{1-6} alkoxy, a C_{1-6} alkyl, a C_{1-6} hydroxyalkyl, a C_{1-6} aminoalkyl, a C_{1-6} alkylamino, an alkylsulfenyl, an alkylsulfinyl, an alkylsulfonyl, an sulfamoyl, or a trifluoromethyl. In certain embodiments, an aromatic

group is substituted at one or more of the para, meta, and/or ortho positions. Examples of aromatic groups comprising substitutions include, but are not limited to, phenyl, 3-halophenyl, 4-halophenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 3-aminophenyl, 4-aminophenyl, 3-methylphenyl, 4-methylphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-trifluoromethoxyphenyl, 3-cyanophenyl, 4-cyanophenyl, dimethylphenyl, naphthyl, hydroxynaphthyl, hydroxymethylphenyl, (trifluoromethyl)phenyl, alkoxyphenyl, 4-morpholin-4-ylphenyl, 4-pyrrolidin-1-ylphenyl, 4-pyrazolylphenyl, 4-triazolylphenyl, and 4-(2-oxopyrrolidin-1-yl)phenyl.

[039] The term "aryl" refers to an aromatic group wherein each of the atoms forming the ring is a carbon atom. Aryl rings may be formed by three, four, five, six, seven, eight, nine, or more than nine carbon atoms. Aryl groups may be optionally substituted.

[040] The term "heteroaryl" refers to an aromatic group wherein at least one atom forming the aromatic ring is a heteroatom. Heteroaryl rings may be formed by three, four, five, six, seven, eight, nine, or more than nine atoms. Heteroaryl groups may be optionally substituted. Examples of heteroaryl groups include, but are not limited to, aromatic C_{3-8} heterocyclic groups comprising one oxygen or sulfur atom or up to four nitrogen atoms, or a combination of one oxygen or sulfur atom and up to two nitrogen atoms, and their substituted as well as benzo- and pyrido-fused derivatives, for example, connected via one of the ring-forming carbon atoms. In certain embodiments, heteroaryl groups are optionally substituted with one or more substituents,

independently selected from halo, hydroxy, amino, cyano, nitro, alkylamido, acyl, C_{1-6}-alkoxy, C_{1-6}-alkyl, C_{1-6}-hydroxyalkyl, C_{1-6}-aminoalkyl, C_{1-6}-alkylamino, alkylsulfenyl, alkylsulfinyl, alkylsulfonyl, sulfamoyl, or trifluoromethyl. Examples of heteroaryl groups include, but are not limited to, unsubstituted and mono- or di-substituted derivatives of furan, benzofuran, thiophene, benzothiophene, pyrrole, pyridine, indole, oxazole, benzoxazole, isoxazole, benzisoxazole, thiazole, benzothiazole, isothiazole, imidazole, benzimidazole, pyrazole, indazole, tetrazole, quinoline, isoquinoline, pyridazine, pyrimidine, purine and pyrazine, furazan, 1,2,3-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, triazole, benzotriazole, pteridine, phenoxazole, oxadiazole, benzopyrazole, quinolizine, cinnoline, phthalazine, quinazoline, and quinoxaline. In some embodiments, the substituents are halo, hydroxy, cyano, O-C_{1-6}-alkyl, C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl, and amino-C_{1-6}-alkyl.

[041] The term "non-aromatic ring" refers to a group comprising a covalently closed ring that does not have a delocalized π-electron system.

[042] The term "cycloalkyl" refers to a group comprising a non-aromatic ring wherein each of the atoms forming the ring is a carbon atom. Cycloalkyl rings may be formed by three, four, five, six, seven, eight, nine, or more than nine carbon atoms. Cycloalkyls may be optionally substituted. In certain embodiments, a cycloalkyl comprises one or more unsaturated bonds. Examples of cycloalkyls include, but are not limited to, cyclopropane, cyclobutane, cyclopentane, cyclopentene, cyclopentadiene, cyclohexane, cyclohexene, 1,3-cyclohexadiene, 1,4-cyclohexadiene, cycloheptane, and

cycloheptene.

[043] The term "non-aromatic heterocycle" refers to a group comprising a non-aromatic ring wherein one or more atoms forming the ring is a heteroatom. Non-aromatic heterocyclic rings may be formed by three, four, five, six, seven, eight, nine, or more than nine atoms. Non-aromatic heterocycles may be optionally substituted. In certain embodiments, non-aromatic heterocycles comprise one or more carbonyl or thiocarbonyl groups such as, for example, oxo- and thio-containing groups. Examples of non-aromatic heterocycles include, but are not limited to, lactams, lactones, cyclic imides, cyclic thioimides, cyclic carbamates, tetrahydrothiopyran, 4*H*-pyran, tetrahydropyran, piperidine, 1,3-dioxin, 1,3-dioxane, 1,4-dioxin, 1,4-dioxane, piperazine, 1,3-oxathiane, 1,4-oxathiin, 1,4-oxathiane, tetrahydro-1,4-thiazine, 2*H*-1,2-oxazine , maleimide, succinimide, barbituric acid, thiobarbituric acid, dioxopiperazine, hydantoin, dihydrouracil, morpholine, trioxane, hexahydro-1,3,5-triazine, tetrahydrothiophene, tetrahydrofuran, pyrroline, pyrrolidine, pyrrolidone, pyrrolidione, pyrazoline, pyrazolidine, imidazoline, imidazolidine, 1,3-dioxole, 1,3-dioxolane, 1,3-dithiole, 1,3-dithiolane, isoxazoline, isoxazolidine, oxazoline, oxazolidine, oxazolidinone, thiazoline, thiazolidine, and 1,3-oxathiolane.

[044] The term "arylalkyl" refers to a group comprising an aryl group bound to an alkyl group.

[045] The term "carbocycloalkyl" refers to a group comprising a carbocyclic cycloalkyl ring. Carbocycloalkyl rings may be formed by three, four, five, six, seven,

eight, nine, or more than nine carbon atoms. Carbocycloalkyl groups may be optionally substituted.

[046] The term "ring" refers to any covalently closed structure. Rings include, for example, carbocycles (*e.g.*, aryls and cycloalkyls), heterocycles (*e.g.*, heteroaryls and non-aromatic heterocycles), aromatics (*e.g.*, aryls and heteroaryls), and non-aromatics (*e.g.*, cycloalkyls and non-aromatic heterocycles). Rings may be optionally substituted. Rings may form part of a ring system.

[047] The term "ring system" refers to two or more rings, wherein two or more of the rings are fused. The term "fused" refers to structures in which two or more rings share one or more bonds.

[048] The substituent"R" appearing by itself and without a number designation refers to a substituent selected from alkyl, cycloalkyl, aryl, heteroaryl (bonded through a ring carbon) and non-aromatic heterocycle (bonded through a ring carbon).

[049] The term "O-carboxy" refers to a group of formula RC(=O)O-.

[050] The term "C-carboxy" refers to a group of formula -C(=O)OR.

[051] The term "acetyl" refers to a group of formula $-C(=O)CH_3$.

[052] The term "trihalomethanesulfonyl" refers to a group of formula $X_3CS(=O)_2$- where X is a halogen.

[053] The term "cyano" refers to a group of formula -CN.

[054] The term "isocyanato" refers to a group of formula -NCO.

[055] The term "thiocyanato" refers to a group of formula -CNS.

[056] The term "isothiocyanato" refers to a group of formula -NCS.

[057] The term "sulfinyl" refers to a group of formula -S(=O)-R.

[058] The term "S-sulfonamido" refers to a group of formula $-S(=O)_2NR$.

[059] The term "N-sulfonamido" refers to a group of formula $RS(=O)_2NH$-.

[060] The term "trihalomethanesulfonamido" refers to a group of formula $X_3CS(=O)_2NR$-.

[061] The term "O-carbamyl" refers to a group of formula -OC(=O)-NR.

[062] The term "N-carbamyl" refers to a group of formula ROC(=O)NH-.

[063] The term "O-thiocarbamyl" refers to a group of formula -OC(=S)-NR.

[064] The term "N-thiocarbamyl" refers to a group of formula ROC(=S)NH-.

[065] The term "C-amido" refers to a group of formula $-C(=O)-NR_2$.

[066] The term "N-amido" refers to a group of formula RC(=O)NH-.

[067] The term "ester" refers to a chemical moiety with formula $-(R)_n$-COOR', where R and R' are independently selected from alkyl, cycloalkyl, aryl, heteroaryl (bonded through a ring carbon) and non-aromatic heterocycle (bonded through a ring carbon), where n is 0 or 1.

[068] The term "amide" refers to a chemical moiety with formula $-(R)_n$-C(O)NHR' or $-(R)_n$-NHC(O)R', where R and R' are independently selected from alkyl, cycloalkyl, aryl, heteroaryl (bonded through a ring carbon) and heteroalicyclic (bonded through a ring carbon), where n is 0 or 1. In certain embodiments, an amide may be an amino acid or a peptide.

[069] The terms "amine," "hydroxy," and "carboxyl" include such groups that have been esterified or amidified. Procedures and specific groups used to achieve esterification and amidification are known to those of skill in the art and can readily be found in reference sources such as Greene and Wuts, Protective Groups in Organic Synthesis, 3rd Ed., John Wiley & Sons, New York, NY, 1999, which is incorporated herein in its entirety.

[070] Unless otherwise indicated, the term "optionally substituted," refers to a group in which none, one, or more than one of the hydrogen atoms has been replaced with one or more group(s) individually and independently selected from: cycloalkyl, aryl, heteroaryl, non-aromatic heterocycle, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, cyano, halo, carbonyl, thiocarbonyl, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, S-sulfonamido, N-sulfonamido, C-carboxy, O-carboxy, isocyanato, thiocyanato, isothiocyanato, nitro, silyl, trihalomethanesulfonyl, and amino, including mono- and di-substituted amino groups, and the protected derivatives of amino groups. Such protective derivatives (and protecting groups that may form such protective derivatives) are known to those of skill in the art and may be found in references such as Greene and Wuts, above. In embodiments in which two or more hydrogen atoms have been substituted, the substituent groups may together form a ring.

[071] The term "carrier" refers to a compound that facilitates the incorporation of another compound into cells or tissues. For example, dimethyl sulfoxide (DMSO) is

a commonly used carrier for improving incorporation of certain organic compounds into cells or tissues.

[072] The term "pharmaceutical agent" refers to a chemical compound or composition capable of inducing a desired therapeutic effect in a patient. In certain embodiments, a pharmaceutical agent comprises an active agent, which is the agent that induces the desired therapeutic effect. In certain embodiments, a pharmaceutical agent comprises a prodrug. In certain embodiments, a pharmaceutical agent comprises inactive ingredients such as carriers, excipients, and the like.

[073] The term "therapeutically effective amount" refers to an amount of a pharmaceutical agent sufficient to achieve a desired therapeutic effect.

[074] The term "prodrug" refers to an pharmaceutical agent that is converted from a less active form into a corresponding more active form *in vivo*.

[075] The term "pharmaceutically acceptable" refers to a formulation of a compound that does not significantly abrogate the biological activity, a pharmacological activity and/or other properties of the compound when the formulated compound is administered to a patient. In certain embodiments, a pharmaceutically acceptable formulation does not cause significant irritation to a patient.

[076] The term "co-administer" refers to administering more than one pharmaceutical agent to a patient. In certain embodiments, co-administered pharmaceutical agents are administered together in a single dosage unit. In certain embodiments, co-administered pharmaceutical agents are administered separately. In

certain embodiments, co-administered pharmaceutical agents are administered at the same time. In certain embodiments, co-administered pharmaceutical agents are administered at different times.

[077] The term "patient" includes human and animal subjects.

[078] The term "substantially pure" means an object species (*e.g.*, compound) is the predominant species present (i.e., on a molar basis it is more abundant than any other individual species in the composition). In certain embodiments, a substantially purified fraction is a composition wherein the object species comprises at least about 50 percent (on a molar basis) of all species present. In certain embodiments, a substantially pure composition will comprise more than about 80%, 85%, 90%, 95%, or 99% of all species present in the composition. In certain embodiments, the object species is purified to essential homogeneity (contaminant species cannot be detected in the composition by conventional detection methods) wherein the composition consists essentially of a single species.

[079] The term "tissue-selective" refers to the ability of a compound to modulate a biological activity in one tissue to a greater or lesser degree than it modulates a biological activity in another tissue. The biological activities in the different tissues may be the same or they may be different. The biological activities in the different tissues may be mediated by the same type of target receptor. For example, in certain embodiments, a tissue-selective compound may modulate a glucocorticoid receptor mediated biological activity in one tissue and fail to modulate, or modulate to a

lesser degree, a glucocorticoid receptor mediated biological activity in another tissue type.

[080] The term "monitoring" refers to observing an effect or absence of any effect. In certain embodiments, one monitors cells after contacting those cells with a compound of the present invention. Examples of effects that may be monitored include, but are not limited to, changes in cell phenotype, cell proliferation, glucocorticoid receptor activity, or the interaction between a glucocorticoid receptor and a natural binding partner.

[081] The term "cell phenotype" refers to physical or biological characteristics. Examples of characteristics that constitute phenotype included, but are not limited to, cell size, cell proliferation, cell differentiation, cell survival, apoptosis (cell death), or the utilization of a metabolic nutrient (*e.g.*, glucose uptake). Certain changes or the absence of changes in cell phenotype are readily monitored using techniques known in the art.

[082] The term "cell proliferation" refers to the rate at which cells divide. The number of cells growing in a vessel can be quantified by a person skilled in the art (*e.g.*, by counting cells in a defined area using a light microscope, or by using laboratory apparatus that measure the density of cells in an appropriate medium). One skilled in that art can calculate cell proliferation by determining the number of cells at two or more times.

[083] The term "contacting" refers to bringing two or more materials into close enough proximity that they may interact. In certain embodiments, contacting can be accomplished in a vessel such as a test tube, a petri dish, or the like. In certain embodiments, contacting may be performed in the presence of additional materials. In certain embodiments, contacting may be performed in the presence of cells. In certain of such embodiments, one or more of the materials that are being contacted may be inside a cell. Cells may be alive or may dead. Cells may or may not be intact.

Certain compounds

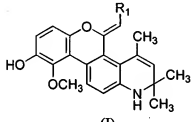
[084] Certain compounds that bind to glucocorticoid receptors and/or modulate an activity of such receptors play a role in health (*e.g.*, normal growth, development, and/or absence of disease). In certain embodiments, selective glucocorticoid receptor modulators and/or binding compounds are useful for treating any of a variety of diseases or conditions.

[085] Certain compounds have been previously described as receptor modulators. *See e.g.*, U. S. Patent Nos. 5,693,646; 6,380,207; 6,506,766; 5,688,810; 5,696,133; Zhi, *et.al. Bioorganic & Medicinal Chemistry Letters* **2000**, *10*, 415-418; Pooley, *et. al., J. Med. Chem.* **1998**, *41*, 3461, the entire disclosures of which are incorporated herein in their entirety.

[086] In certain embodiments, the present invention provides selective glucocorticoid receptor modulators. In certain embodiments, the invention provides selective glucocorticoid receptor binding agents. In certain embodiments, the invention

provides methods of making and methods of using selective glucocorticoid receptor modulators and/or selective glucocorticoid binding agents. In certain embodiments, selective glucocorticoid modulators are agonists, partial agonists, and/or antagonists for the glucocorticoid receptor.

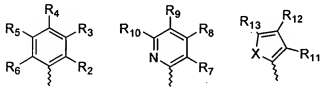
[087] In certain embodiments, the present invention relates to a compound of Formula I:



(I)

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

[088] In certain embodiments, R_1 is selected from Formula II, III, and IV:



(II) (III) (IV)

[089] In certain embodiments, R_2 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-CONR_{14}R_{15}$, $-OR_{16}$, $-SR_{16}$, $-SO_2NR_{14}R_{15}$, and an optionally substituted aryl. In certain embodiments in which R_2 is an optionally

substituted aryl, R_2 is an optionally substituted phenyl. In certain of such embodiments, R_2 is an optionally substituted phenyl that is optionally substituted with a substituent selected from hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[090] In certain embodiments, R_3 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-OR_{16}$, $-SR_{16}$ and an optionally substituted aryl. In certain embodiments in which R_3 is an optionally substituted aryl, R_3 is an optionally substituted phenyl. In certain of such embodiments, R_3 is an optionally substituted phenyl that is optionally substituted with a substituent selected from hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[091] In certain embodiments, R_4 is selected from hydrogen, F, Cl, Br, CN, $-OR_{16}$, a ring, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[092] In certain embodiments, R_2 and R_3 together form an optionally substituted 5-6 member ring and R_4 is selected from hydrogen, F, Cl, Br, CN, $-OR_{16}$, a ring, $-SO_2NR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl. In certain embodiments, R_3 and R_4 together form an optionally substituted 4-6 member ring and R_2 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally

substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, -OR_{16}, -SR_{16} ,-$SO_2NR_{14}R_{15}$, and an optionally substituted aryl.

[093] In certain embodiments, R_5 is selected from hydrogen, F, Cl, Br, optionally substituted C_1-C_4 alkyl, and OCH_3.

[094] In certain embodiments, R_6 is selected from hydrogen and F.

[095] In certain embodiments, R_7 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl. In certain embodiments in which R_7 is an optionally substituted aryl, R_7 is an optionally substituted phenyl. In certain of such embodiments, R_7 is an optionally substituted phenyl that is optionally substituted with a substituent selected from hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[096] In certain embodiments, R_8 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -OR_{16}, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[097] In certain embodiments, R_9 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[098] In certain embodiments, R_7 and R_8 together form an optionally substituted 5-6 member ring and R_9 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl. In certain embodiments, R_8 and R_9 together form an optionally substituted 4-6 member ring and R_7 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl.

[099] In certain embodiments, R_{10} is selected from hydrogen, F, Cl, CH_3, and OCH_3.

[0100] In certain embodiments, R_{11} is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl. In certain embodiments in which R_{11} is an optionally substituted aryl, R_{11} is an optionally substituted phenyl. In certain of such embodiments, R_{11} is an optionally substituted phenyl that is optionally substituted with a substituent selected from hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[0101] In certain embodiments, R_{12} is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -OR_{16}, a phenyl that is optionally substituted

with hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[0102] In certain embodiments, R_{13} is selected from hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[0103] In certain embodiments, R_{11} and R_{12} together form an optionally substituted 5-6 member ring and R_{13} is selected from hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl. In certain embodiments, R_{12} and R_{13} together form an optionally substituted 4-6 member ring and R_{11}, is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl.

[0104] In certain embodiments, R_{14} and R_{15} are each independently selected from hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[0105] In certain embodiments, R_{14} and R_{15} together form an optionally substituted 4-7 member ring.

[0106] In certain embodiments, R_{16} is selected from hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, and an optionally substituted aryl. In certain

embodiments in which R_{16} is an optionally substituted aryl, R_{16} is an optionally substituted phenyl. In certain of such embodiments, R_{16} is an optionally substituted phenyl that is optionally substituted with a substituent selected from hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

[0107] In certain embodiments, X is selected from O, S, and NR_{17}.

[0108] In certain embodiments, R_{17} is selected from hydrogen and an optionally substituted C_1-C_4 alkyl.

[0109] In certain embodiments, at least one position selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen. In certain embodiments, at least one position selected from R_7, R_8, R_9, and R_{10} is not hydrogen. In certain embodiments, if R_4 is F, then at least one position selected from R_2, R_3, R_5 and R_6 is not hydrogen. In certain embodiments, if R_3 is F, then at least one position selected from R_2, R_4, R_5, and R_6 is not hydrogen. In certain embodiments, if any two positions selected from R_2, R_3, R_4, R_5, and R_6 are both F, then at least one of the other three positions selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen.

[0110] In certain embodiments, a compound of Formula I is a selective glucocorticoid receptor modulator. In certain embodiments, a compound of Formula I is a selective glucocorticoid receptor agonist. In certain embodiments, a compound of Formula I is a selective glucocorticoid receptor antagonist. In certain embodiments, a compound of Formula I is a selective glucocorticoid receptor partial agonist. In certain

embodiments, a compound of Formula I is a tissue-specific selective glucocorticoid modulator. In certain embodiments, a compound of Formula I is a gene-specific selective glucocorticoid modulator. In certain embodiments, a compound of Formula I is a selective glucocorticoid receptor binding compound.

[0111] In certain embodiments, the invention provides compounds selected from:

(Z)-5-(3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',5'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-

chromeno[3,4-f]quinoline;

(Z)-5-(4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-trifluoromehoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-trifluoromehoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-trifluorothiomethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-fluoro-3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-fluoro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',4'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-chloro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-di(trifluoromethy)lbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-fluoro-5'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',4',5'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-ethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-fluoro-2'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-6'-fluorobenzylidene)1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-isopropylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-

chromeno[3,4-f]quinoline;

(Z)-5-(4'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-fluoro-4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(6'-methyl-pyridinylmethylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-methyl-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-benzyloxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-methy-4'-fluorolbenzylidene)-1,2-dihydro-9-(3-methyl-4-fluorobenzoyloxy)-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-cyclohexylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-chloro-4'-trifluoromethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',6'-difluoro-3'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-3',6'-difluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-methyl-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-fluoro-4'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3'-difluoro-4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3',5',6'-tetrafluoro-4'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-dimethylaminocarbonyfuranylmethylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-vinylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-Chloro-6'-fluoro-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-

2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-trifluoromethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-trifluorothiobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',4'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-chloro-2'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-(4"-methylbenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-di-tert-butylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2",2"-difluoroethoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',5'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3"-thiophene)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-diethylaminocarbonylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4",4",4"-trifluorobutoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2",4"-difluorophenyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3"-pyridyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3"-benzenecarbaldehyde)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',4'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(diethylamino)carbonyl-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(diethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(methylbenzylamino)carbonyl-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(di-methylamino)carbonyl-5'-bromo-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2"-fluoroethoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2",2",3",3"-tetrafluoropropoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-fluorobenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2"-fluorobenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(pyrolidinecarbonylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(pyrolidinecarbonyl-5'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(di-methylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(pyrolidinecarbonyl-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(pyrolidinecarbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-fluorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(morpholinecarbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-fluoro-benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-dimethylcarbonyl-3'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(4"-methylpiperazine)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-methyl-3'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-di-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(piperidineamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-dimethylaminosulphonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(ethylmethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(cyclohexylmethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-cyanobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-

chromeno[3,4-f]quinoline;

(Z)-5-(2',3',5',6'-tetrafluoro-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-hydroxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(piperidinesulphonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-napthylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-methyl-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2-cyclohexyl-4-methyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',5'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2-cyclohexyl-4-methyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3'-ethylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-hydroxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-cyano-3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-chloro-2'-cyanobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-bromo-2'-cyano-benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-chloro-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-3',4'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-cyano-3'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-methyl-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-cyano-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4',5'-difluoro-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3",5"-dichlophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-methoxy)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3",4"-dichlorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-

2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-methyl)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-chloro)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3"-trifluoromethoxy)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4- f]quinoline;

(Z)-5-(2'-(3'-(dimethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(ethylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(morpholinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-cyclohexylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(pyrrolidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2"-dimethoxyethyl)aminocarbonylthiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(allylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(piperidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-piperidinecarbonyl-4"-(1,3-dioxan)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(5'-(diethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(5'-(pyrrolidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(5'-(2"-methylpyrrolidinecarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(5'-morpholinecarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-dimethylaminocarbonyl-5'-methylfuranylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-cyclohexylmethylaminocarbonyl-5'-methylfuranylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

. In certain embodiments, the invention provides a pharmaceutically acceptable salt, ester, amide, or prodrug of any of those compounds.

[0112] In the following table, the inventors contemplate any combination of the following Markush group and those described above for the various variables.

Table A. Table of Markush Groups by Variable

	Markush Group A	Markush Group B	Markush Group C	Markush Group D
R_2	hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-CONR_{14}R_{15}$, $-OR_{16}$, $-SR_{16}$, $-SO_2NR_{14}R_{15}$, and an optionally substituted aryl	hydrogen, F, Cl, optionally substituted C_1-C_4 alkyl, $-CONR_{14}R_{15}$	hydrogen, $-CONR_{14}R_{15}$	H
	R_2 and R_3 together form an optionally substituted 5-6 member ring			
R_3	hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-OR_{16}$, $-SR_{16}$ and an optionally substituted aryl	hydrogen, F, Cl, optionally substituted C_1-C_4 alkyl, optionally substituted C_1-C_4 haloalkyl, $-OR_{16}$	optionally substituted C_1-C_2 alkyl, optionally substituted C_1-C_2 haloalkyl, $-OR_{16}$	H

	R_2 and R_3 together form an optionally substituted 5-6 member ring			
	R_3 and R_4 together form an optionally substituted 4-6 member ring			
R_4	hydrogen, F, Cl, Br, CN, $-OR_{16}$, a ring, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl	hydrogen, F, Cl, $-OR_{16}$, optionally substituted C_1-C_4 alkyl	hydrogen, F, optionally substituted C_1-C_2 alkyl	H
	R_3 and R_4 together form an optionally substituted 4-6 member ring			
R_5	hydrogen, F, Cl, Br, optionally substituted C_1-C_4 alkyl, and OCH_3	hydrogen, F, Cl, Br, optionally substituted C_1-C_2 alkyl	CH_3	H

R_6	hydrogen and F	F		H
R_7	hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl	H, F, optionally substituted C_1-C_4 alkyl	CH_3	H
	R_7 and R_8 together form an optionally substituted 5-6 member ring			

R_8	hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-OR_{16}$, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl	H, F, optionally substituted C_1-C_4 alkyl	CH_3	H
	R_7 and R_8 together form an optionally substituted 5-6 member ring			
	R_8 and R_9 together form an optionally substituted 4-6 member ring			

R_9	hydrogen, F, Cl, Br, CN, an optionally substituted C1-C4 alkyl, an optionally substituted C1-C4 haloalkyl, and an optionally substituted C1-C4 heteroalkyl	H, F, optionally substituted C_1-C_4 alkyl	CH_3	H
	R_8 and R_9 together form an optionally substituted 4-6 member ring			
R_{10}	hydrogen, F, Cl, CH_3, and OCH_3	H, F, CH_3	CH_3	H
R_{11}	hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl	hydrogen, F, Cl, -$CONR_{14}R_{15}$	-$CONR_{14}R_{15}$	H
	R_{11} and R_{12} together form an optionally substituted 5-6 member ring			

R_{12}	hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -OR_{16}, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl	H, F, Cl, optionally substituted C_1-C_4 alkyl	CH_3	H
	R_{11} and R_{12} together form an optionally substituted 5-6 member ring			
	R_{12} and R_{13} together form an optionally substituted 4-6 member ring			

R_{13}	R_{13} is selected from hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl	hydrogen, F, Cl, $-CONR_{14}R_{15}$	$-CONR_{14}R_{15}$	H
	R_{12} and R_{13} together form an optionally substituted 4-6 member ring			
R_{14}	hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl	H, optionally substituted C_1-C_4 alkyl	CH_3	H
	R_{14} and R_{15} together form an optionally substituted 4-7 member ring			

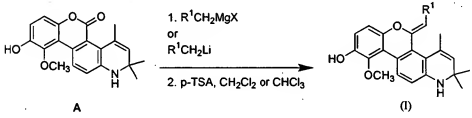
R_{15}	hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl	H, optionally substituted C_1-C_4 alkyl	CH_3	H
	R_{14} and R_{15} together form an optionally substituted 4-7 member ring			
R_{16}	R_{16} is selected from hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, and an optionally substituted aryl	H, optionally substituted C_1-C_4 alkyl	CH_3	H
R_{17}	hydrogen and an optionally substituted C_1-C_4 alkyl	H, optionally substituted C_1-C_2 alkyl	CH_3	H
X	O, S, and NR_{17}	O, S	S	O

[0113] Certain compounds of the present inventions may exist as stereoisomers including optical isomers. The present disclosure is intended to include all stereoisomers and both the racemic mixtures of such stereoisomers as well as the individual enantiomers that may be separated according to methods that are known in the art.

Certain Synthesis Methods

[0114] In certain embodiments, synthesis of compounds of the present invention is accomplished using Scheme I.

Scheme I



A (I)

[0115] Certain schemes for synthesizing a compound having structure A have been previously discussed. *See e.g.*, US Patent No. 6,506,766. The process of Scheme I involves the addition of an organometallic reagent, for example an organomagnesium or organolithium reagent, to the compound of structure A. Dehydration of the intermediate with an acid, such as p-toluenesulfonic acid, affords compounds of the generic Formula I.

[0116] In certain embodiments, the invention provides a salt corresponding to any of the compounds provided herein. In certain embodiments, the invention provides

a salt corresponding to a selective glucocorticoid receptor modulator or selective glucocorticoid binding agent. In certain embodiments, a salt is obtained by reacting a compound with an inorganic acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. In certain embodiments, a salt is obtained by reacting a compound with a base to form a salt such as an ammonium salt, an alkali metal salt, such as a sodium or a potassium salt, an alkaline earth metal salt, such as a calcium or a magnesium salt, a salt of organic bases such as dicyclohexylamine, N-methyl-D-glucamine, tris(hydroxymethyl)methylamine, and salts with amino acids such as arginine, lysine, and the like.

[0117] In certain embodiments, one or more carbon atoms of a compound of the present invention is replaced with silicon. *See e.g.*, WO 03/037905A1; Tacke and Zilch, Endeavour, New Series, 10, 191-197 (1986); Bains and Tacke, Curr. Opin. Drug Discov Devel. Jul:6(4):526-43(2003). In certain embodiments, compounds of the present invention comprising one or more silicon atoms possess certain desired properties, including, but not limited to, greater stability and/or longer half-life in a patient, when compared to the same compound in which none of the carbon atoms have been replaced with a silicon atom.

Certain Assays

[0118] In certain embodiments, compounds of the present invention are capable of modulating activity of glucocorticoid receptors in a "co-transfection" assay (also

called a "cis-trans" assay), which has been discussed previously. *See e.g.*, Evans *et al.*, *Science*, 240:889-95 (1988); U.S. Patent Nos. 4,981,784 and 5,071,773; Pathirana *et al.*, "Nonsteroidal Human Progesterone Receptor Modulators from the Marie Alga Cymopolia Barbata," *Mol. Pharm. 47*:630-35 (1995)). Modulating activity in a co-transfection assay has been shown to correlate with *in vivo* modulating activity. Thus, in certain embodiments, such assays are predictive of *in vivo* activity. *See, e.g*, Berger *et al.*, *J. Steroid Biochem. Molec. Biol.* 41:773 (1992).

[0119] In certain co-transfection assays, two different co-transfection plasmids are prepared. In the first co-transfection plasmid, cloned cDNA encoding an intracellular receptor (*e.g.*, glucocorticoid receptor) is operatively linked to a constitutive promoter (*e.g.*, the SV 40 promoter). In the second co-transfection plasmid, cDNA encoding a reporter protein, such as firefly luciferase (LUC), is operatively linked to a promoter that is activated by a receptor-dependant activation factor. Both co-transfection plasmids are co-transfected into the same cells. Expression of the first co-transfection plasmid results in production of the intracellular receptor protein. Activation of that intracellular receptor protein (*e.g.*, by binding of an agonist) results in production of a receptor-dependant activation factor for the promoter of the second co-transfection plasmid. That receptor-dependant activation factor in turn results in expression of the reporter protein encoded on the second co-transfection plasmid. Thus, reporter protein expression is linked to activation of the receptor. Typically, that reporter activity can be conveniently measured (*e.g.*, as increased luciferase production).

[0120] Certain co-transfection assays can be used to identify agonists, partial agonists, and/or antagonists of intracellular receptors. In certain embodiments, to identify agonists, co-transfected cells are exposed to a test compound. If the test compound is an agonist or partial agonist, reporter activity is expected to increase compared to co-transfected cells in the absence of the test compound. In certain embodiments, to identify antagonists, the cells are exposed to a known agonist (*e.g.*, glucocorticoid for the glucocorticoid receptor) in the presence and absence of a test compound. If the test compound is an antagonist, reporter activity is expected to decrease relative to that of cells exposed only to the known agonist.

[0121] In certain embodiments, compounds of the invention are used to detect the presence, quantity and/or state of receptors in a sample. In certain of such embodiments, samples are obtained from a patient. In certain embodiments, compounds are radio- or isotopically-labeled. For example, compounds of the present invention that selectively bind glucocorticoid receptors may be used to determine the presence of such receptors in a sample, such as cell homogenates and lysates.

Certain Pharmaceutical Agents

[0122] In certain embodiments, at least one selective glucocorticoid receptor modulator, or pharmaceutically acceptable salt, ester, amide, and/or prodrug thereof, either alone or combined with one or more pharmaceutically acceptable carriers, forms a pharmaceutical agent. Techniques for formulation and administration of compounds of the present invention may be found for example, in "Remington's Pharmaceutical

Sciences," Mack Publishing Co., Easton, PA, 18th edition, 1990.

[0123] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention is prepared using known techniques, including, but not limited to mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or tabletting processes.

[0124] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention is a liquid (*e.g.*, a suspension, elixir and/or solution). In certain of such embodiments, a liquid pharmaceutical agent comprising one or more compounds of the present invention is prepared using ingredients known in the art, including, but not limited to, water, glycols, oils, alcohols, flavoring agents, preservatives, and coloring agents.

[0125] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention is a solid (*e.g.*, a powder, tablet, and/or capsule). In certain of such embodiments, a solid pharmaceutical agent comprising one or more compounds of the present invention is prepared using ingredients known in the art, including, but not limited to, starches, sugars, diluents, granulating agents, lubricants, binders, and disintegrating agents.

[0126] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention is formulated as a depot preparation. Certain of such depot preparations are typically longer acting than non-depot preparations. In certain embodiments, such preparations are administered by implantation (for example

subcutaneously or intramuscularly) or by intramuscular injection. In certain embodiments, depot preparations are prepared using suitable polymeric or hydrophobic materials (for example an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

[0127] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention comprises a delivery system. Examples of delivery systems include, but are not limited to, liposomes and emulsions. Certain delivery systems are useful for preparing certain pharmaceutical agents including those comprising hydrophobic compounds. In certain embodiments, certain organic solvents such as dimethylsulfoxide are used.

[0128] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention comprises one or more tissue-specific delivery molecules designed to deliver the pharmaceutical agent to specific tissues or cell types. For example, in certain embodiments, pharmaceutical agents include liposomes coated with a tissue-specific antibody.

[0129] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention comprises a co-solvent system. Certain of such co-solvent systems comprise, for example, benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. In certain embodiments, such co-solvent systems are used for hydrophobic compounds. A non-limiting example of such a co-solvent system is the VPD co-solvent system, which is a solution of absolute

ethanol comprising 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant Polysorbate 80™ , and 65% w/v polyethylene glycol 300. The proportions of such co-solvent systems may be varied considerably without significantly altering their solubility and toxicity characteristics. Furthermore, the identity of co-solvent components may be varied: for example, other surfactants may be used instead of Polysorbate 80™; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, *e.g.*, polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose.

[0130] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention comprises a sustained-release system. A non-limiting example of such a sustained-release system is a semipermeable matrix of solid hydrophobic polymers. In certain embodiments, sustained-release systems may, depending on their chemical nature, release compounds over a period of hours, days, weeks or months.

[0131] Certain compounds used in pharmaceutical agent of the present invention may be provided as pharmaceutically acceptable salts with pharmaceutically compatible counterions. Pharmaceutically compatible salts may be formed with many acids, including but not limited to hydrochloric, sulfuric, acetic, lactic, tartaric, malic, succinic, *etc.*

[0132] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention comprises an active ingredient in a therapeutically

effective amount. In certain embodiments, the therapeutically effective amount is sufficient to prevent, alleviate or ameliorate symptoms of a disease or to prolong the survival of the subject being treated. Determination of a therapeutically effective amount is well within the capability of those skilled in the art.

[0133] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention is formulated as a prodrug. In certain embodiments, prodrugs are useful because they are easier to administer than the corresponding active form. For example, in certain instances, a prodrug may be more bioavailable (*e.g.*, through oral administration) than is the corresponding active form. In certain instances, a prodrug may have improved solubility compared to the corresponding active form. In certain embodiments, a prodrug is an ester. In certain embodiments, such prodrugs are less water soluble than the corresponding active form. In certain instances, such prodrugs possess superior transmittal across cell membranes, where water solubility is detrimental to mobility. In certain embodiments, the ester in such prodrugs is metabolically hydrolyzed to carboxylic acid. In certain instances the carboxylic acid containing compound is the corresponding active form. In certain embodiments, a prodrug comprises a short peptide (polyaminoacid) bound to an acid group. In certain of such embodiments, the peptide is metabolized to form the corresponding active form.

[0134] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention is useful for treating a conditions or disorder in a

mammalian, and particularly in a human patient. Suitable administration routes include, but are not limited to, oral, rectal, transmucosal, intestinal, enteral, topical, suppository, through inhalation, intrathecal, intraventricular, intraperitoneal, intranasal, intraocular and parenteral (*e.g.*, intravenous, intramuscular, intramedullary, and subcutaneous). In certain embodiments, pharmaceutical intrathecals are administered to achieve local rather than systemic exposures. For example, pharmaceutical agents may be injected directly in the area of desired effect (*e.g.*, in the renal or cardiac area).

[0135] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present invention is administered in the form of a dosage unit (*e.g.*, tablet, capsule, bolus, etc.). In certain embodiments, such dosage units comprise a selective glucocorticoid receptor modulator in a dose from about 1 μg/kg of body weight to about 50 mg/kg of body weight. In certain embodiments, such dosage units comprise a selective glucocorticoid receptor modulator in a dose from about 2 μg/kg of body weight to about 25 mg/kg of body weight. In certain embodiments, such dosage units comprise a selective glucocorticoid receptor modulator in a dose from about 10 μg/kg of body weight to about 5 mg/kg of body weight. In certain embodiments, pharmaceutical agents are administered as needed, once per day, twice per day, three times per day, or four or more times per day. It is recognized by those skilled in the art that the particular dose, frequency, and duration of administration depends on a number of factors, including, without limitation, the biological activity desired, the condition of the patient, and tolerance for the pharmaceutical agent.

[0136] In certain embodiments, a pharmaceutical agent comprising a compound of the present invention is prepared for oral administration. In certain of such embodiments, a pharmaceutical agent is formulated by combining one or more compounds of the present invention with one or more pharmaceutically acceptable carriers. Certain of such carriers enable compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient. In certain embodiments, pharmaceutical agents for oral use are obtained by mixing one or more compounds of the present invention and one or more solid excipient. Suitable excipients include, but are not limited to, fillers, such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). In certain embodiments, such a mixture is optionally ground and auxiliaries are optionally added. In certain embodiments, pharmaceutical agents are formed to obtain tablets or dragee cores. In certain embodiments, disintegrating agents (*e.g.*, cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof, such as sodium alginate) are added.

[0137] In certain embodiments, dragee cores are provided with coatings. In certain of such embodiments, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or

solvent mixtures. Dyestuffs or pigments may be added to tablets or dragee coatings.

[0138] In certain embodiments, pharmaceutical agents for oral administration are push-fit capsules made of gelatin. Certain of such push-fit capsules comprise one or more compounds of the present invention in admixture with one or more filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In certain embodiments, pharmaceutical agents for oral administration are soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. In certain soft capsules, one or more compounds of the present invention are be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added.

[0139] In certain embodiments, pharmaceutical agents are prepared for buccal administration. Certain of such pharmaceutical agents are tablets or lozenges formulated in conventional manner.

[0140] In certain embodiments, a pharmaceutical agent is prepared for administration by injection (*e.g.*, intravenous, subcutaneous, intramuscular, etc.). In certain of such embodiments, a pharmaceutical agent comprises a carrier and is formulated in aqueous solution, such as water or physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. In certain embodiments, other ingredients are included (*e.g.*, ingredients that aid in solubility or serve as preservatives). In certain embodiments, injectable suspensions are prepared using appropriate liquid carriers, suspending agents and the like. Certain

pharmaceutical agents for injection are presented in unit dosage form, *e.g.*, in ampoules or in multi-dose containers. Certain pharmaceutical agents for injection are suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Certain solvents suitable for use in pharmaceutical agents for injection include, but are not limited to, lipophilic solvents and fatty oils, such as sesame oil, synthetic fatty acid esters, such as ethyl oleate or triglycerides, and liposomes. Aqueous injection suspensions may contain substances that increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, such suspensions may also contain suitable stabilizers or agents that increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

[0141] In certain embodiments, a pharmaceutical agent is prepared for transmucosal administration. In certain of such embodiments penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

[0142] In certain embodiments, a pharmaceutical agent is prepared for administration by inhalation. Certain of such pharmaceutical agents for inhalation are prepared in the form of an aerosol spray in a pressurized pack or a nebulizer. Certain of such pharmaceutical agents comprise a propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In certain embodiments using a pressurized aerosol, the dosage unit may be determined

with a valve that delivers a metered amount. In certain embodiments, capsules and cartridges for use in an inhaler or insufflator may be formulated. Certain of such formulations comprise a powder mixture of a compound of the invention and a suitable powder base such as lactose or starch.

[0143] In certain embodiments, a pharmaceutical agent is prepared for rectal administration, such as a suppositories or retention enema. Certain of such pharmaceutical agents comprise known ingredients, such as cocoa butter and/or other glycerides.

[0144] In certain embodiments, a pharmaceutical agent is prepared for topical administration. Certain of such pharmaceutical agents comprise bland moisturizing bases, such as ointments or creams. Exemplary suitable ointment bases include, but are not limited to, petrolatum, petrolatum plus volatile silicones, lanolin and water in oil emulsions such as Eucerin™, available from Beiersdorf (Cincinnati, Ohio). Exemplary suitable cream bases include, but are not limited to, Nivea™ Cream, available from Beiersdorf (Cincinnati, Ohio), cold cream (USP), Purpose Cream™, available from Johnson & Johnson (New Brunswick, New Jersey), hydrophilic ointment (USP) and Lubriderm™, available from Pfizer (Morris Plains, New Jersey).

[0145] In certain embodiments, the formulation, route of administration and dosage for a pharmaceutical agent of the present invention can be chosen in view of a particular patient's condition. (*See e.g.*, Fingl *et al.* 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p. 1). In certain embodiments, a pharmaceutical agent is

administered as a single dose. In certain embodiments, a pharmaceutical agent is administered as a series of two or more doses administered over one or more days.

[0146] In certain embodiments, a pharmaceutical agent of the present invention is administered to a patient between about 0.1% and 500%, more preferably between about 25% and 75% of an established human dosage. Where no human dosage is established, a suitable human dosage may be inferred from ED_{50} or ID_{50} values, or other appropriate values derived from *in vitro* or *in vivo* studies.

[0147] In certain embodiments, a daily dosage regimen for a patient comprises an oral dose of between 0.1 mg and 2000 mg of a compound of the present invention. In certain embodiments, a daily dosage regimen is administered as a single daily dose. In certain embodiments, a daily dosage regimen is administered as two, three, four, or more than four doses.

[0148] In certain embodiments, a pharmaceutical agent of the present invention is administered by continuous intravenous infusion. In certain of such embodiments, from 0.1 mg to 500 mg of a composition of the present invention is administered per day.

[0149] In certain embodiments, a pharmaceutical agent of the invention is administered for a period of continuous therapy. For example, a pharmaceutical agent of the present invention may be administered over a period of days, weeks, months, or years.

[0150] Dosage amount, interval between doses, and duration of treatment may be adjusted to achieve a desired effect. In certain embodiments, dosage amount and interval between doses are adjusted to maintain a desired concentration on compound in a patient. For example, in certain embodiments, dosage amount and interval between doses are adjusted to provide plasma concentration of a compound of the present invention at an amount sufficient to achieve a desired effect. In certain of such embodiments the plasma concentration is maintained above the minimal effective concentration (MEC). In certain embodiments, pharmaceutical agents of the present invention are administered with a dosage regimen designed to maintain a concentration above the MEC for 10-90% of the time, between 30-90% of the time, or between 50-90% of the time.

[0151] In certain embodiments in which a pharmaceutical agent is administered locally, the dosage regimen is adjusted to achieve a desired local concentration of a compound of the present invention.

[0152] In certain embodiments, a pharmaceutical agent may be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack may for example comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. The pack or dispenser may also be accompanied with a notice associated with the container in form prescribed by a governmental agency regulating the manufacture, use, or sale of pharmaceuticals, which notice is reflective of approval

by the agency of the form of the drug for human or veterinary administration. Such notice, for example, may be the labeling approved by the U.S. Food and Drug Administration for prescription drugs, or the approved product insert. Compositions comprising a compound of the invention formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

[0153] In certain embodiments, a pharmaceutical agent is in powder form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

Certain Combination Therapies

[0154] In certain embodiments, one or more pharmaceutical agents of the present invention are co-administered with one or more other pharmaceutical agents. In certain embodiments, such one or more other pharmaceutical agents are designed to treat the same disease or condition as the one or more pharmaceutical agents of the present invention. In certain embodiments, such one or more other pharmaceutical agents are designed to treat a different disease or condition as the one or more pharmaceutical agents of the present invention. In certain embodiments, such one or more other pharmaceutical agents are designed to treat an undesired effect of one or more pharmaceutical agents of the present invention. In certain embodiments, one or more pharmaceutical agents of the present invention is co-administered with another pharmaceutical agent to treat an undesired effect of that other pharmaceutical agent. In certain embodiments, one or more pharmaceutical agents of the present invention and

one or more other pharmaceutical agents are administered at the same time. In certain embodiments, one or more pharmaceutical agents of the present invention and one or more other pharmaceutical agents are administered at the different times. In certain embodiments, one or more pharmaceutical agents of the present invention and one or more other pharmaceutical agents are prepared together in a single formulation. In certain embodiments, one or more pharmaceutical agents of the present invention and one or more other pharmaceutical agents are prepared separately.

[0155] Examples of pharmaceutical agents that may be co-administered with a pharmaceutical agent of the present invention include, but are not limited to, analgesics (*e.g.*, acetaminophen); anti-inflammatory agents, including, but not limited to non-steroidal anti-inflammatory drugs (*e.g.*, ibuprofen, COX-1 inhibitors, and COX-2, inhibitors); salicylates; antibiotics; antivirals; antifungal agents; antidiabetic agents (*e.g.*, biguanides, glucosidase inhibitors, insulins, sulfonylureas, and thiazolidenediones); adrenergic modifiers; diuretics; hormones (*e.g.*, anabolic steroids, androgen, estrogen, calcitonin, progestin, somatostan, and thyroid hormones); immunomodulators; muscle relaxants; antihistamines; osteoporosis agents (e.g., biphosphonates, calcitonin, and estrogens); prostaglandins, antineoplastic agents; psychotherapeutic agents; sedatives; poison oak or poison sumac products; antibodies; and vaccines.

Certain Indications

[0156] In certain embodiments, the invention provides methods of treating a patient comprising administering a compound of the present invention. In certain

embodiments, such patient suffers from a glucocorticoid receptor mediated condition.

[0157] Exemplary conditions that may be treated with compounds of the present invention included, but are not limited to, inflammation (including, but not limited to, rheumatoid arthritis, asthma, lupus, osteoarthritis, rhinosinusitis, inflammatory bowel disease, polyarteritis nodosa, Wegener's granulomatosis, giant cell arteritis, allergic rhinitis, urticaria, hereditary angioedema, chronic obstructive pulmonary disease, tendonitis, bursitis, autoimmune chronic active hepatitis, cirrhosis), transplant rejection, psoriasis, dermatitus, autoimmune disorders, malignancies (leukemia, myelomas, lymphomas), acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, granulomatous disease, immune proliferation/apotosis, HPA axis suppression and regulation, hypercortisolemia, Th1/Th2 cytokine related disorders, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hyperglycemia, cerebral edema, thrombocytopenia, Little's syndrome, Addison's disease, cystic fibrosis, myasthenia gravis, autoimmune hemolytic anemia, uveitis, pemphigus vulgaris, multiple sclerosis, nasal polyps, sepsis, infections (bacterial, viral, rickettsial, parasitic), type II diabetes, obesity, metabolic syndrome, depression, schizophrenia, mood disorders, Cushing's syndrome, anxiety, sleep disorders, memory and learning enhancement, and glaucoma.

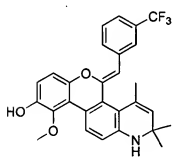
[0158] In certain embodiments, a compound of the present invention is used to treat arthritis. In certain embodiments, a compound of the present invention is used to treat asthma, including chronic asthma and/or acute asthma. In certain embodiments, a compound of the present invention is used to treat multiple sclerosis.

[0159] In certain embodiments, a compound of the present invention is used to treat cancer. Certain exemplary cancers include, but are not limited to, breast cancer, colorectal cancer, gastric carcinoma, glioma, head and neck squamous cell carcinoma, papillary renal carcinoma, leukemia, lymphoma, Li-Fraumeni syndrome, malignant pleural mesothelioma, melanoma, multiple myeloma, non-small cell lung cancer, synovial sarcoma, thyroid carcinoma, and transitional cell carcinoma of urinary bladder.

Examples

[0160] The following examples, including experiments and results achieved, are provided for illustrative purposes only and are not to be construed as limiting the present invention.

Example 1

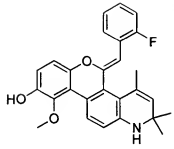


(Z)-5-(3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 11, structure 1 of Scheme I, where R^1 = 3'-trifluoromethylphenyl)

[0161] General Method 1: To a flame-dried 2-neck, 10 mL round bottom flask

fitted with a reflux condenser was added magnesium turnings (28 mg, 2.0 mmol) and diethyl ether (3 mL). A solution of 3-trifluoromethylbenzyl bromide (478 mg, 2.0 mmol) in diethyl ether was added to the slurry of magnesium turnings. After 1h, a solution of 9-hydroxy-10-methoxy-2,2,4-trimethyl-1,2-dihydro-5H-chromeno[3,4-f]quinoline-5-one (Compound A, Scheme I) (30 mg, 0.09 mmol) in diethyl ether (1 mL) was added. After 18 h, the reaction was quenched with ammonium chloride (3 mL), extracted with ethyl acetate (2 X 10 mL), washed with brine (2 X 10 mL), dried over magnesium sulfate, filtered, and concentrated. The crude product was purified by precipitation from dichloromethane/hexanes and collected by filtration. The product was then dissolved in dichloromethane and treated with p-toluenesulfonic acid (catalytic) and followed by TLC (0.1 % triethylamine/dichloromethane). After 20 min, the solution was filtered on silica gel, washed with dichloromethane and concentrated. The crude product was then purified by flash chromatography (0.1 % triethylamine/dichloromethane) to afford the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.6 Hz, 1H), 8.10 (s, 1H), 7.91-7.84 (m, 1H), 7.48-7.41 (m, 2-overlapping signals, 2H), 6.87 (d, J = 10.8 Hz, 1H), 6.85 (d, J = 10.8 Hz, 1H), 6.69 (d, J = 8.6 Hz, 1H), 5.65 (s, 1H), 5.56 (s, 1H), 5.53 (s, 1H), 4.21 (br s, 1H), 3.78 (s, 3H), 2.10 (s, 3H), 1.37 (br s, 6H).

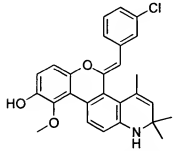
Example 2



(Z)-5-(2'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 12, structure 1 of Scheme I, where R^1 = 2'-fluorophenyl)

[0162] This compound was prepared according to General Method 1 (Example 1) from 2-fluorobenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (m, 1H), 8.17 (d, J = 8.8 Hz, 1H), 7.19 (m, 2H), 7.07 (m, 1H), 6.85 (d, J = 8.8 Hz, 1H), 6.69 (d, J = 8.3 Hz, 1H), 6.74 (d, J = 8.8 Hz, 1H), 5.92 (s, 1H), 5.53 (s, 1H), 3.78 (s, 3H), 2.12 (d, J = 1.0 Hz, 3H), 1.29 (br s, 6H).

Example 3

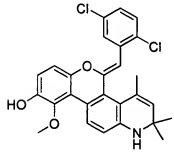


(Z)-5-(3'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 13, structure 1 of Scheme I, where R^1 = 3'-

chlorophenyl)

[0163] This compound was prepared according to General Method 1 (Example 1) from 3-chlorobenzyl chloride. ^{1}H NMR (400 MHz, CD_3OD) δ 8.28 (d, J = 8.6 Hz), 7.42 (s, 1H), 7.27-7.18 (m, 2H), 6.82-6.70 (m, 4H), 5.54 (s, 1H), 5.52 (s, 1H), 3.76 (s, 3H), 2.06 (s, 3H), 1.31 (br s, 6H).

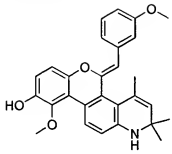
Example 4



(Z)-5-(2',5'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 14, structure 1 of Scheme I, where R^1 = 2',5'-dichlorophenyl)

[0164] This compound was prepared according to General Method 1 (Example 1) from 2,5-dichlorobenzyl chloride. ^{1}H NMR (400 MHz, CD_3OD) δ 8.39-8.32 (m, 2-overlapping signals, 2H), 7.39 (d, J = 8.6 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 6.81-6.75 (m, 3H), 6.07 (s, 1H), 5.53 (s, 1H), 3.79 (s, 3H), 2.09 (s, 3H), 1.31 (br s, 6H).

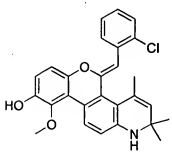
Example 5



(Z)-5-(3'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 15, structure 1 of Scheme I, where R^1 = 3'-methoxyphenyl)

[0165] This compound was prepared according to General Method 1 (Example 1) from 3-methoxybenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.28 (d, J = 8.6 Hz), 7.42 (s, 1H), 7.27-7.18 (m, 2H), 6.82-6.70 (m, 4H), 5.54 (s, 1H), 5.52 (s, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 2.06 (s, 3H), 1.31 (br s, 6H).

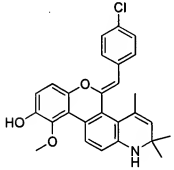
Example 6



(Z)-5-(2'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 16, structure 1 of Scheme I, where R^1 = 2'-chlorophenyl)

[0166] This compound was prepared according to General Method 1 (Example 1) from 2-chlorobenzyl chloride. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.40 (dd, J = 2.9, 2.9 Hz, 1H), 8.32 (d, J = 7.2 Hz, 1H), 7.40 (m, 1H), 7.22 (m, 1H), 6.84 (m, 2H), 6.84 (d, J = 8.6 Hz, 1H), 6.15 (s, 1H), 5.91 (s, 1H), 5.61 (s, 1H), 5.52 (s, 1H), 3.77 (s, 3H), 2.08 (s, 3H), 1.35 (br s, 6H).

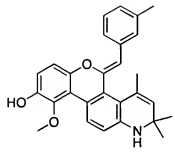
Example 7



(Z)-5-(4'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 17, structure 1 of Scheme I, where R^1 = 4'-chlorophenyl)

[0167] This compound was prepared according to General Method 1 (Example 1) from 4-chlorobenzyl bromide. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.29 (d, J = 7.2 Hz, 1H), 7.80 (m, 2H), 7.75 (s, 1H), 7.37 (m, 2H), 6.92 (m, 1H), 6.67 (m, 2H), 5.87 (s, 1H), 5.64 (s, 1H), 5.21 (s, 1H), 3.77 (s, 3H), 2.08 (s, 3H), 1.30 (br s, 6H).

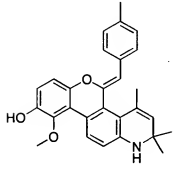
Example 8



(Z)-5-(3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 18, structure 1 of Scheme I, where R^1 = 3'-methylphenyl)

[0168] This compound was prepared according to General Method 1 (Example 1) from 3-methylbenzyl bromide. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.28 (d, J = 7.2 Hz, 1H), 7.74 (s, 1H), 7.60 (m, 2H), 7.16 (m, 2H), 6.87 (m, 1H), 6.77 (m, 1H), 5.83 (br s, 1H), 5.61 (s, 1H), 5.51 (br s, 1H), 3.76 (s, 3H), 2.34 (s, 3H), 2.08 (s, 3H), 1.30 (br s, 6H).

Example 9

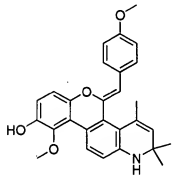


(Z)-5-(4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 19, structure 1 of Scheme I, where R^1 = 4'-

methylphenyl)

[0169] This compound was prepared according to General Method 1 (Example 1) from 4-methylbenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.25 (d, J = 8.9 Hz, 1H), 7.60-7.53 (m, 2-overlapping signals, 2H), 7.10-7.08 (m, 2-overlapping signals, 2H), 6.78 (d, J = 8.6 Hz, 1H), 6.72-6.68 (m, 2-overlapping signals, 2H), 5.50 (s, 1H), 5.46 (s, 1H), 3.72 (s, 3H), 2.29 (s, 3H), 2.02 (s, 3H), 1.25 (br s, 6H).

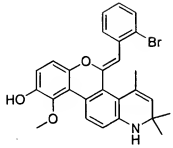
Example 10



(Z)-5-(4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 20, structure 1 of Scheme I, where R^1 = 4'-methoxyphenyl)

[0170] This compound was prepared according to General Method 1 (Example 1) from 4-methoxybenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.24 (d, J = 8.6 Hz, 1H), 7.68-7.55 (m, 2-overlapping signals, 2H), 6.92-6.86 (m, 2-overlapping signals, 2H), 6.78 (d, J = 8.6 Hz, 1H), 6.72-6.66 (m, 2-overlapping signals, 2H), 5.50-5.47 (m, 2-overlapping signals, 2H), 3.78 (s, 3H), 3.73 (s, 3H), 2.03 (s, 3H), 1.29 (br s, 6H).

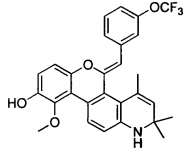
Example 11



(Z)-5-(2'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 21, structure 1 of Scheme I, where R^1 = 2'-bromophenyl)

[0171] This compound was prepared according to General Method 1 (Example 1) from 2-bromobenzyl bromide. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.41 (dd, J = 7.2, 7.2 Hz, 1H), 8.33 (d, J = 6.9 Hz, 1H), 7.80 (s, 1H), 7.61 (dd, J = 8.0, 1.1 Hz, 1H), 7.43 (m, 1H), 7.14 (m, 1H), 6.86 (m, 2H), 6.78 (m,1H), 6.15 (s, 1H), 5.92 (br s, 1H), 5.51 (br s, 1H), 3.80 (s, 3H), 2.08 (s, 3H), 1.31 (br s, 6H).

Example 12

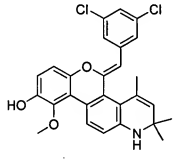


(Z)-5-(3'-trifluoromehoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline (Compound 22, structure 1 of Scheme I, where R^1 = 3'-trifluoromethoxyphenyl)

[0172] This compound was prepared according to General Method 1 (Example 1) from 3-trifluoromethoxybenzyl bromide. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.31 (d, J = 7.2 Hz, 1H), 7.88 (s, 1H), 7.81 (s, 1H), 7.65 (m, 1H), 7.47 (m, 1H), 7.16 (m, 1H), 6.84 (m, 2H), 5.91 (br s, 1H), 5.71 (s, 1H), 5.27 (s, 1H), 3.79 (s, 3H), 2.08 (s, 3H), 1.32 (br s, 6H).

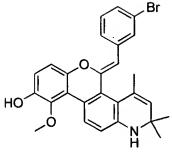
Example 13



(Z)-5-(3',5'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 23, structure 1 of Scheme I, where R^1 = 3',5'-dichlorophenyl)

[0173] This compound was prepared according to General Method 1 (Example 1) from 3,5-dichlorobenzyl chloride. ^{1}H NMR (400 MHz, CD_3OD) δ 8.33 (d, J = 8.8 Hz, 1H), 7.67 (d, J = 1.8 Hz, 1H), 7.23 (t, J = 1.8 Hz, 1H), 6.83-6.75 (m, 4H), 5.53 (s, 1H), 5.52 (s, 1H), 3.77 (s, 3H), 2.04 (s, 3H), 1.31 (br s, 6H).

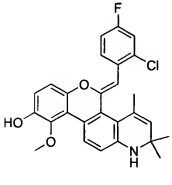
Example 14



(Z)-5-(3'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 24, structure 1 of Scheme I, where R^1 = 3'-bromophenyl)

[0174] This compound was prepared according to General Method 1 (Example 1) from 3-bromobenzyl bromide. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.32 (d, J = 7.2 Hz, 1H), 8.01 (s, 1H), 7.80 (s, 1H), 7.80 (m, 1H), 7.38 (m, 1H), 7.31 (m, 1H), 6.86 (m, 2H), 6.78 (m,1H), 5.64 (s, 1H), 5.50 (s, 1H), 3.79 (s, 3H), 2.08 (s, 3H), 1.32 (br s, 6H).

Example 15

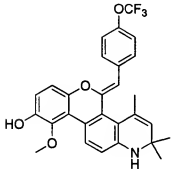


(Z)-5-(2'-chloro-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 25, structure 1 of Scheme I, where

R^1 = 2'-chloro-4'-fluorophenyl)

[0175] This compound was prepared according to General Method 1 (Example 1) from 2-chloro-4-fluorobenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.35-8.28 (m, 2H), 7.18 (dd, J = 8.8, 2.7 Hz, 1H), 7.11 (dt, J = 8.5, 2.6 Hz, 1H), 6.81-6.73 (m, 2-overlapping signals, 2H), 6.70 (d, J = 8.7 Hz, 1H), 6.01 (s, 1H), 5.48 (s, 1H), 3.75 (s, 3H), 2.06 (s, 3H), 1.28 (br s, 6H).

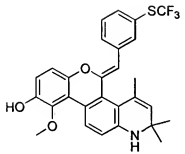
Example 16



(Z)-5-(4'-trifluoromehoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 26, structure 1 of Scheme I, where R^1 = 4'-trifluoromethoxyphenyl)

[0176] This compound was prepared according to General Method 1 (Example 1) from 4-trifluoromethoxybenzyl bromide. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.30 (d, J = 7.2 Hz, 1H), 7.90 (m, 2H), 7.32 (m, 1H), 6.92 (d, J = 5.5 Hz, 1H), 6.79 (m, 2H), 5.69 (br s, 1H), 5.51 (s, 1H), 5.27 (s, 1H), 3.76 (s, 3H), 2.08 (s, 3H), 1.32 (br s, 6H).

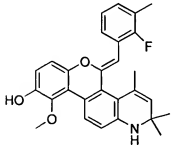
Example 17



(Z)-5-(3'-trifluorothiomethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 27, structure 1 of Scheme I, where R^1 = 3'-trifluorothiophenylphenyl)

[0177] This compound was prepared according to General Method 1 (Example 1) from 3-thiotrifluoromethylbenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.30 (d, *J* = 8.7 Hz, 1H), 8.16 (s, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.50-7.42 (m, 2H), 6.81-6.74 (m, 3H), 5.59 (s, 1H), 5.51 (s, 1H), 3.75 (s, 3H), 2.05 (s, 3H), 1.30 (br s, 6H).

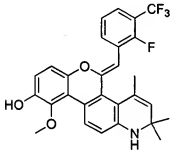
Example 18



(Z)-5-(2'-fluoro-3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 28, structure 1 of Scheme I, where R^1 = 2'-fluoro-3'-methylphenyl)

[0178] This compound was prepared according to General Method 1 (Example 1) from 2-fluoro-3-methylbenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.29 (d, J = 8.7 Hz, 1H), 8.11-8.02 (m, 1H), 7.08-6.99 (m, 2H), 6.79-6.70 (m, 3H), 5.84 (s, 1H), 5.49 (s, 1H), 3.75 (s, 3H), 2.23 (s, 3H), 2.05 (s, 3H), 1.29 (br s, 6H).

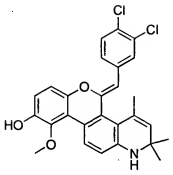
Example 19



(Z)-5-(2'-fluoro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 29, structure 1 of Scheme I, where R^1 = 2'-fluoro-3'trifluoromethylphenyl)

[0179] This compound was prepared according to General Method 1 (Example 1) from 2-fluoro-3-trifluorobenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) 8.55 (t, J = 7.0 Hz, 1H), 8.36 (d, J = 8.6 Hz, 1H), 7.48 (t, J = 7.0 Hz, 1H), 7.36 (t, J = 7.9 Hz, 1H), 6.80-6.85 (m, 2H), 6.76 (d, J = 8.6 Hz, 1H), 5.87 (s, 1H), 5.55 (s, 1H), 3.78 (s, 3H), 2.07 (s, 3H), 1.32 (br s, 6H).

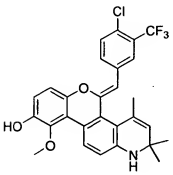
Example 20



(Z)-5-(3',4'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 30, structure 1 of Scheme I, where R^1 = 3',4'-dichlorophenyl)

[0180] This compound was prepared according to General Method 1 (Example 1) from 3,4-dichlorobenzyl chloride. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (m, 1H), 8.17 (d, J = 8.8 Hz, 1H), 7.19 (m, 2H), 6.85 (d, J = 8.8 Hz, 1H), 6.69 (d, J = 8.3 Hz, 1H), 6.74 (d, J = 8.8 Hz, 1H), 5.92 (s, 1H), 5.53 (s, 1H), 3.78 (s, 3H), 2.12 (d, J = 1.0 Hz, 3H), 1.29 (br s, 6H).

Example 21

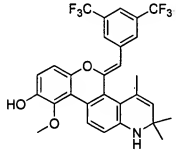


(Z)-5-(4'-chloro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-

2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 31, structure 1 of Scheme I, where R^1 = 4'-chloro-3'-trifluoromethylphenyl)

[0181] This compound was prepared according to General Method 1 (Example 1) from 4-chloro-3-trifluoromethylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.55 (d, J = 7.1 Hz, 1H), 8.36 (d, J = 8.7 Hz, 1H), 8.19 (s, 1H), 7.48 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 7.9 Hz, 1H), 6.82 (m, 2H), 6.76 (s, 1H), 5.56 (s, 1H), 3.74 (s, 3H), 2.16 (s, 3H), 1.36 (br s, 6H).

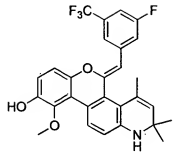
Example 22



(Z)-5-(3',5'-di(trifluoromethyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 32, structure 1 of Scheme I, where R^1 = 3',5'-di(trifluoromethyl)phenyl)

[0182] This compound was prepared according to General Method 1 (Example 1) from 3,5-di(trifluromethyl)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.36 (d, J = 8.9 Hz, 1H), 8.29 (s, 2H), 7.74 (s, 1H), 6.82 (d, J = 8.6 Hz, 1H), 6.77 (s, 2H), 5.76 (s, 1H), 5.56 (s, 1H), 3.78 (s, 3H), 2.07 (s, 3H), 1.33 (br s, 6H).

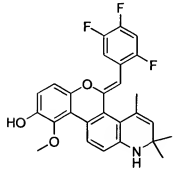
Example 23



(Z)-5-(3'-fluoro-5'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 33, structure 1 of Scheme I, where R^1 = 3'-fluoro-5'-trifluoromethylphenyl)

[0183] This compound was prepared according to General Method 1 (Example 1) from 3-fluoro-5-trifluoromethylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.35 (d, J = 8.9 Hz, 1H), 7.84 (s, 1H), 7.74 (d, J = 10.4 Hz, 1H), 7.24 (d, J = 8.6 Hz, 1H), 6.82 (d, J = 3.4 Hz, 1H), 6.80 (d, J = 3.1 Hz, 1H), 6.78 (d, J = 8.9 Hz, 1H), 5.66 (s, 1H), 5.43 (s, 1H), 3.77 (s, 3H), 2.05 (s, 3H), 1.32 (br s, 6H).

Example 24

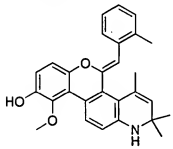


(Z)-5-(2',4',5'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline (Compound 34, structure 1 of Scheme I, where R^1 = 2',4',5'-trifluorophenyl)

[0184] This compound was prepared according to General Method 1 (Example 1) from 2,4,5-trifluorobenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17-8.20 (m, 2H), 6.85-6.93 (m, 3H), 6.71 (d, J = 8.6 Hz, 1H), 5.54 (s, 1H), 4.72 (s, 1H), 3.80 (s, 3H), 2.08 (s, 3H), 1.35 (br s, 6H).

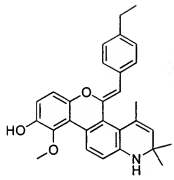
Example 25



(Z)-5-(2'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 35, structure 1 of Scheme I, where R^1 = 2'-methylphenyl)

[0185] This compound was prepared according to General Method 1 (Example 1) from 2-methylbenzyl bromide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (m, 2H), 7.25 (m, 2H), 7.18 (m, 2H), 6.85-6.93 (m, 2H), 6.71 (m, 1H), 5.86 (s, 1H), 5.52 (m, 1H), 5.30 (s, 1H), 3.80 (s, 3H), 2.28 (s, 3H), 2.14 (s, 3H), 1.35 (br s, 6H).

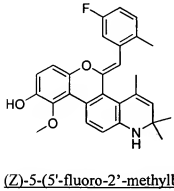
Example 26



(Z)-5-(4'-ethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 36, structure 1 of Scheme I, where R^1 = 4'-ethylphenyl)

[0186] This compound was prepared according to General Method 1 (Example 1) from 4-ethylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.6 Hz), 7.63 (d, J = 8.2 Hz, 2H), 7.18 (d, J = 8.2 Hz, 2H), 6.81 (d, J = 8.9 Hz, 1H), 6.74 (d, J = 8.9 Hz, 1H), 6.72 (d, J = 8.9 Hz, 1H), 5.53 (s, 1H), 5.50 (s, 1H), 3.75 (s, 3H), 2.63 (q, J = 7.63 Hz, 2H), 2.05 (s, 3H), 1.30 (br s, 6H), 1.24 (t, J = 7.63 Hz, 3H).

Example 27

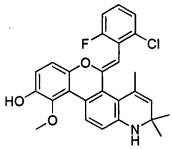


(Z)-5-(5'-fluoro-2'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline (Compound 37, structure 1 of Scheme I, where R^1 = 5'-fluoro-2'methylphenyl)

[0187] This compound was prepared according to General Method 1 (Example 1) from 5-fluoro-2-methylbenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.03 (m, 1H), 7.95 (m, 1H), 7.88 (m, 1H), 7.67 (m, 1H), 7.60 (m, 2H), 7.55 (m, 1H), 6.92 (d, 1H), 5.30 (s, 1H), 4.92 (s, 1H), 3.79 (s, 3H) 2.36 (s, 3H), 2.08 (s, 3H), 1.32 (br s, 6H).

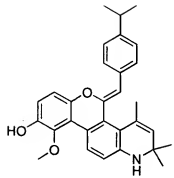
Example 28



(Z)-5-(2'-chloro-6'-fluorobenzylidene)1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 38, structure 1 of Scheme I, where R^1 = 2'-chloro-6'-fluorophenyl)

[0188] This compound was prepared according to General Method 1 (Example 1) from 2-chloro-6-fluorobenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.33 (d, J = 8.8 Hz, 1H), 7.27-7.20 (m, 2H), 7.12-7.07 (m, 1H), 6.78 (d, J = 8.7 Hz, 1H), 6.62 (d, J = 8.6 Hz, 1H), 6.47 (d, J = 8.8 Hz, 1H), 5.55 (s, 1H), 5.49 (s, 1H), 3.76 (s, 3H), 2.18 (s, 3H), 1.28 (br s, 6H).

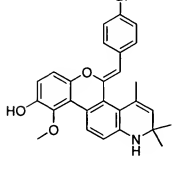
Example 29



(Z)-5-(4'-isopropylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 39, structure 1 of Scheme I, where R^1 = 4'-isopropylphenyl)

[0189] This compound was prepared according to General Method 1 (Example 1) from 4-isopropylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.6 Hz, 1H), 7.64 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.2 Hz, 1H), 6.82 (d, J = 8.6 Hz, 1H), 6.74 (d, J = 8.6 Hz, 1H), 6.72 (d, J = 8.9 Hz, 1H), 5.53 (s, 1H), 5.50 (s, 1H), 3.75 (s, 3H), 2.89 (septet, J = 7.0 Hz, 1H), 2.05 (s, 3H), 1.30 (br s, 6H), 1.25 (d, J = 6.7 Hz, 1H).

Example 30

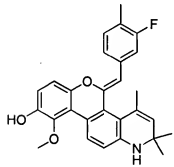


(Z)-5-(4'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-

chromeno[3,4-f]quinoline (Compound 40, structure 1 of Scheme I, where R^1 = 4'-bromophenyl)

[0190] This compound was prepared according to General Method 1 (Example 1) from 4-bromobenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.27 (d, J = 8.6 Hz, 1H), 7.65-7.58 (m, 2-overlapping signals, 2H), 7.49-7.41 (m, 2-overlapping signals, 2H), 6.81 (d, J = 8.7 Hz, 1H), 6.74 (d, J = 8.6 Hz, 1H), 6.71 (d, J = 8.8 Hz, 1H), 5.51 (s, 1H), 5.49 (s, 1H), 3.74 (s, 3H), 2.02 (s, 3H), 1.28 (br s, 6H).

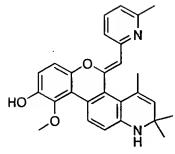
Example 31



(Z)-5-(3'-fluoro-4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 41, structure 1 of Scheme I, where R^1 = 3'-fluoro-4'-methylphenyl)

[0191] This compound was prepared according to General Method 1 (Example 1) from 3-fluoro-4-methylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.30 (d, J = 8.9 Hz, 1H), 7.54 (dd, J = 11.9, 1.2 Hz, 1H), 7.28 (d, J = 8.2, 1.5 Hz, 1H), 7.18 (t, J = 8.1 Hz, 1H), 6.83 (d, J = 8.9 Hz, 1H), 6.76 (m, 2 H), 5.53 (m, 2H), 3.76 (s, 3H), 2.26 (s, 3H), 2.04 (s, 3H), 1.31 (br s, 6H).

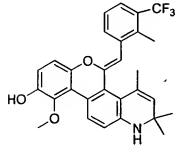
Example 32



(Z)-5-(6'-methyl-pyridinylmethylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 42, structure 1 of Scheme I, where R^1 = 3'-methylpyridine)

[0192] This compound was prepared according to General Method 2 (Example 65) from 2,6-lutidine. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, J = 8.5 Hz, 1H), 8.24 (d, J = 8.2 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.07 (d, J = 7.7 Hz, 1H), 6.87 (d, J = 8.9 Hz, 1H), 6.80 (d, J = 8.5 Hz, 1H), 6.74 (d, J = 8.6 Hz, 1H), 5.87 (s, 1H), 5.52 (d, J = 1.2 Hz, 1H), 3.77 (s, 3H), 2.48 (s, 3H), 2.07 (d, J = 1.2 Hz, 3H), 1.33 (br s, 6H).

Example 33

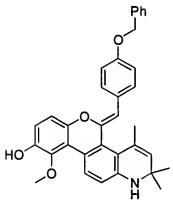


(Z)-5-(2'-methyl-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 43, structure 1 of Scheme I,

where R^1 = 2'-methyl-3'-trifluoromethylphenyl)

[0193] This compound was prepared according to General Method 1 (Example 1) from 2-methyl-3-trifluromethylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.33 (d, J = 8.6 Hz, 1H), 8.24 (d, J = 7.9 Hz, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.37 (t, J = 7.9 Hz, 1H), 6.79 (d, J = 8.6 Hz, 1H), 6.70 (d, J = 8.6 Hz, 1H), 6.66 (d, J = 8.9 Hz, 1H), 5.88 (s, 1H), 5.52 (s, 1H), 3.77 (s, 3H), 2.33 (s, 3H), 2.11 (s, 3H), 1.31 (br s, 6H).

Example 34

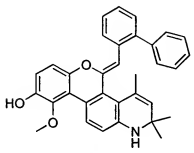


(Z)-5-(4'-benzyloxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 44, structure 1 of Scheme I, where R^1 = 4'-benzyloxyphenyl)

[0194] This compound was prepared according to General Method 1 (Example 1) from 4-benzyloxybenzyl bromide. ^{1}H NMR (500MHz, $CDCl_3$) δ 8.14 (d, J = 8.6 Hz, 1H), 7.72 (d, J = 8.9 Hz, 2H), 7.45 (d, J = 7.0 Hz, 2H), 7.40 (dd, J = 7.6, 7.0 Hz, 2H), 7.34 (d, J = 7.6 Hz, 1H), 6.98 (d, J = 8.9 Hz, 2H), 6.89 (d, J = 8.9 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 6.65 (d, J = 8.6 Hz, 1H), 5.56 (s, 1H), 5.31 (s, 1H), 5.10 (s, 2H), 3.78 (s,

3H), 2.10 (s, 3H), 1.35 (br s, 6H).

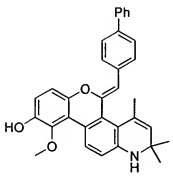
Example 35



(Z)-5-(2'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 46, structure 1 of Scheme I, where R^1 = 2'-biphenyl)

[0195] This compound was prepared according to General Method 1 (Example 1) from 2-phenylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.51 (d, J = 7.1 Hz, 1H), 8.25 (d, J = 7.3 Hz, 1H), 7.42 (m, 1H), 7.38 (m, 2H), 7.22 (m, 4H), 6.82 (d, 1H), 6.72 (d, J = 7.2 Hz, 1H), 6.67 (d, 1H), 5.65 (s, 1H), 5.25 (s, 1H), 3.76 (s, 3H), 1.88 (s, 3H), 2.25 (s, 3H), 1.32 (br s, 6H).

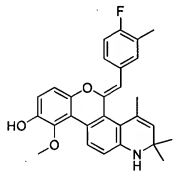
Example 36



(Z)-5-(4'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 47, structure 1 of Scheme I, where R^1 = 4'-biphenyl)

[0196] This compound was prepared according to General Method 1 (Example 1) from 4-phenylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.31 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 8.2 Hz, 2H), 6.65 (d, J = 8.6 Hz, 2H), 7.63 (d, J = 8.6 Hz, 2H), 7.42 (dd, J = 8.2, 7.3 Hz, 2H), 7.31 (t, J = 7.30, 1H), 6.87 (d, J = 8.9 Hz, 1H), 6.78 (d, J = 8.6 Hz, 1H), 6.75 (d, J = 8.9 Hz, 1H), 5.61 (s, 1H), 5.53 (s, 1H), 3.77 (s, 3H), 2.08 (s, 3H), 1.32 (br s, 6H).

Example 37

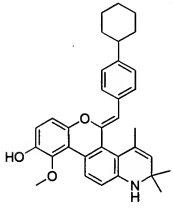


(Z)-5-(3'-methy-4'-fluorolbenzylidene)-1,2-dihydro-9-(3-methyl-4-fluorobenzoyloxy)-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 48, structure 1 of Scheme I, where R^1 = 4'-fluoro-3'-methylphenyl)

[0197] This compound was prepared according to General Method 1 (Example 1) from 4-fluoro-3-methylbenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 7.1 Hz, 1H), 7.52 (m, 2H), 6.97 (m, 1H), 6.88 (m, 1H), 6.68 (d, 1H), 5.55 (m, 3H), 4.18

(m, 1H), 3.78 (s, 3H), 2.31 (s, 3H), 2.09 (s, 3H), 1.88 (s, 3H), 2.25 (s, 3H), 1.48 (br s, 6H).

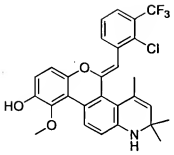
Example 38



(Z)-5-(4'-cyclohexylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 49, structure 1 of Scheme I, where R^1 = 4'-cyclohexylphenyl)

[0198] This compound was prepared according to General Method 1 (Example 1) from 4-cyclohexylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.6 Hz, 1H), 7.62 (d, J = 8.2 Hz, 2H), 7.18 (d, J = 8.2 Hz, 2H), 6.82 (d, J = 8.9 Hz, 1H), 6.74 (d, J = 9.5 Hz, 1H), 6.72 (d, J = 8.9 Hz, 1H), 5.53 (s, 1H), 5.50 (s, 1H), 3.75 (s, 3H), 2.50-2.46 (m, 1H), 2.05 (s, 3H), 1.84 (d, J = 9.2 Hz, 4H), 1.75 (d, J = 12.8 Hz, 1H), 1.38-1.49 (m, 5H), 1.31 (br s, 6H).

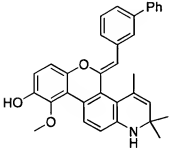
Example 39



(Z)-5-(2'-chloro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 51, structure 1 of Scheme I, where R^1 = 2'-chloro-3'-trifluoromethylphenyl)

[0199] This compound was prepared according to General Method 1 (Example 1) from 2-chloro-3-trifluorobenzyl bromide. ^{1}H NMR (500 MHz, CD_3Cl) δ 8.44 (d, J = 8.6 Hz, 1H), 8.21 (d, J = 7.9 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.39 (t, J = 7.9 Hz, 1H), 6.82 (d, J = 8.6 Hz, 1H), 6.72 (d, J = 8.6 Hz, 1H), 6.11 (s, 1H), 5.59 (s, 1H), 5.30 (s, 1H), 3.81 (s, 3H), 2.13 (s, 3H), 1.36 (br s, 6H).

Example 40

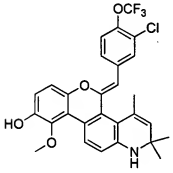


(Z)-5-(3'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 52, structure 1 of Scheme I, where R^1 = 2'-

biphenyl)

[0200] This compound was prepared according to General Method 1 (Example 1) from 3-phenylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.30 (d, J = 8.6 Hz, 1H), 8.00 (s, 1H), 7.64-7.68 (m, 3H), 7.41-7.48 (m, 4H), 7.36 (t, J = 7.3 Hz, 1H), 6.72-6.81 (m, 3H), 5.65 (s, 1H), 5.54 (s, 1H), 3.78 (s, 3H), 2.10 (s, 3H), 1.32 (br s, 6H).

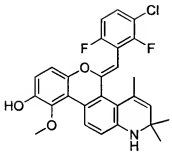
Example 41



(Z)-5-(3'-chloro-4'-trifluoromethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 54, structure 1 of Scheme I, where R^1 = 3'-chloro-4'-trifluoromethoxyphenyl)

[0201] This compound was prepared according to General Method 1 (Example 1) from 3-chloro-4-trifluoromethoxybenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.31 (d, J = 8.6 Hz, 1H), 7.95 (s, 1H), 7.68 (d, J = 8.6 Hz, 1H), 7.37 (d, J = 8.6 Hz, 1H), 6.82 (d, J = 8.9 Hz, 1H), 6.77 (d, J = 8.6 Hz, 1H), 6.74 (d, J = 8.9 Hz, 1H), 5.55 (s, 1H), 5.51 (s, 1H), 3.75 (s, 3H), 2.03 (s, 3H), 1.29 (br s, 6H).

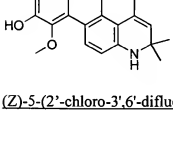
Example 42



(Z)-5-(2',6'-difluoro-3'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 55, structure 1 of Scheme I, where R^1 = 3'-chloro-2',6'-difluorophenyl)

[0202] This compound was prepared according to General Method 1 (Example 1) from 3-chloro-2,6-difluorobenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.37 (d, J = 8.6 Hz, 1H), 7.35-7.40 (m, 1H), 6.99 (dt, J = 8.9, 1.8 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 6.68 (d, J = 8.9 Hz, 1H), 6.55 (d, J = 8.9 Hz, 1H), 5.53 (s, 1H), 5.52 (s, 1H), 3.78 (s, 3H), 2.17 (s, 3H), 1.30 (br s, 6H).

Example 43

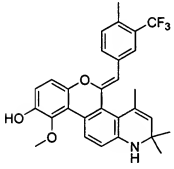


(Z)-5-(2'-chloro-3',6'-difluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline (Compound 56, structure 1 of Scheme I, where R^1 = 2'-chloro-3',6'-difluorophenyl)

[0203] This compound was prepared according to General Method 1 (Example 1) from 2-chloro-3,6-difluorobenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.35 (d, *J* = 8.9 Hz, 1H), 7.18-7.14 (m, 2H), 6.80 (d, *J* = 8.6 Hz, 1H), 6.63 (d, *J* = 8.9 Hz, 1H), 6.49 (d, *J* = 8.6 Hz, 1H), 5.55 (s, 1H), 5.50 (s, 1H), 3.76 (s, 3H), 2.19 (s, 3H), 1.29 (br s, 6H).

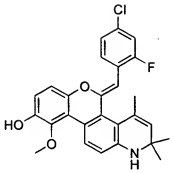
Example 44



(Z)-5-(4'-methyl-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 58, structure 1 of Scheme I, where R^1 = 4'-methyl-3'-trifluoromethylphenyl)

[0204] This compound was prepared according to General Method 1 (Example 1) from 4-methyl-3-trifluorobenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.26 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 1.5 Hz, 1H), 7.00 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.80-6.78 (m, 2H), 6.73-6.71 (m, 2H), 5.95 (s, 2H), 5.50-5.48 (m, 2H), 3.75 (s, 3H), 2.04 (d, *J* = 1.2 Hz, 3H), 1.30 (br s, 6H).

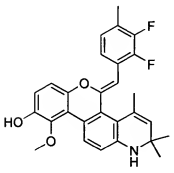
Example 45



(Z)-5-(2'-fluoro-4'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 59, structure 1 of Scheme I, where R^1 = 4'-chloro-2'-fluorophenyl)

[0205] This compound was prepared according to General Method 1 (Example 1) from 4-chloro-2-fluorobenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (app t, J = 8.4 Hz, 1H), 8.18 (d, J = 8.5 Hz, 1H), 7.16 (d, J = 8.5 Hz, 1H), 7.06 (dd, J = 10.4, 2.1 Hz, 1H), 6.84 (s, 1H), 6.69 (d, J = 8.5 Hz, 1H), 5.83 (s, 1H), 5.70 (s, 1H), 5.53 (s, 1H), 4.22 (br s, 1H), 3.79 (s, 3H), 2.09 (s, 3H), 1.36 (br s, 6H).

Example 46

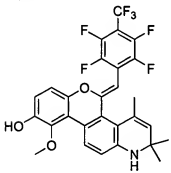


(Z)-5-(2',3'-difluoro-4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline (Compound 60, structure 1 of Scheme I, where R^1 = 2',3'-difluoro-4'-methylphenyl)

[0206] This compound was prepared according to General Method 1 (Example 1) from 2,3-difluoro-4-methylbenzyl bromide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, J = 7.4 Hz, 2H), 8.18 (d, J = 8.4 Hz, 1H), 7.95 (m, 1H), 6.95 (m, 1H), 6.84 (s, 1H), 6.70 (d, J = 8.5 Hz, 1H), 5.85 (s, 1H), 5.58 (s, 1H), 4.22 (br s, 1H), 3.79 (s, 3H), 2.31 (s, 3H), 2.10 (s, 3H), 1.36 (br s, 6H).

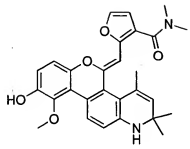
Example 47



(Z)-5-(2',3',5',6'-tetrafluoro-4'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 61, structure 1 of Scheme I, where R^1 = 2',3',5',6'-tetrafluoro-4'-trifluoromethylphenyl)

[0207] This compound was prepared according to General Method 1 (Example 1) from 2,3,5,6-tetrafluoro-4-trifluoromethylbenzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.37 (d, J = 8.6 Hz, 1H), 6.99 (dt, J = 8.9, 1.8 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 6.68 (d, J = 8.9 Hz, 1H), 6.55 (d, J = 8.9 Hz, 1H), 5.53 (s, 1H), 3.78 (s, 3H), 2.17 (s, 3H), 1.30 (br s, 6H).

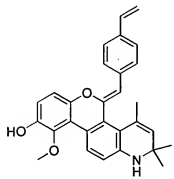
Example 48



(Z)-5-(2'-(3'-dimethylaminocarbonyfuranylmethylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 62, structure 1 of Scheme I, where R^1 = 3'-dimethylaminocarbonylfuranyl)

[0208] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(N,N-dimethyl)furanamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.35 (d, J = 8.8 Hz, 1H), 7.53 (d, J = 2.0 Hz, 1H), 6.80 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 8.8 Hz, 1H), 6.71 (d, J = 8.8 Hz, 1H) 6.56 (d, J = 2.0 Hz, 1H), 5.65 (s, 1H), 5.51 (d, J = 1.5 Hz, 1H), 3.75 (s, 3H), 3.02 (s, 6H), 2.08 (d, J = 1.5 Hz, 3H), 1.29 (br s, 6H).

Example 49

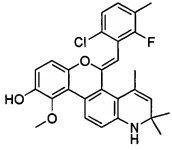


(Z)-5-(4'-vinylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-

chromeno[3,4-f]quinoline (Compound 63, structure 1 of Scheme I, where R^1 = 4'-vinylphenyl)

[0209] This compound was prepared according to General Method 1 (Example 1) from 4-vinylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.29 (d, J = 8.6 Hz, 1H), 7.69 (d, J = 8.2 Hz, 2H), 7.41 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.6 Hz, 1H), 6.69-6.76 (m, 3H), 5.77 (d, J = 17.7 Hz, 1H), 5.56 (s, 1H), 5.51 (s, 1H), 5.20 (d, J = 11.0 Hz, 1H), 3.76 (s, 3H), 2.06 (s, 3H), 1.31 (br s, 6H).

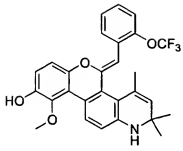
Example 50



(Z)-5-(2'-Chloro-6'-fluoro-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 64, structure 1 of Scheme I, where R^1 = 2'-chloro-6'-fluoro-5'-methylphenyl)

[0210] This compound was prepared according to General Method 1 (Example 1) from 2-chloro-6-fluoro-5-methylbenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 8.5 Hz, 1H), 7.26 (m, 1H, obscured by solvent), 6.96 (app t, J = 8.9 Hz, 1H), 6.72 (m, 2H), 6.63 (d, J = 8.9 Hz, 1H), 5.66 (s, 1H), 5.53-5.51 (m, 2H), 4.20 (br s, 1H), 3.81 (s, 3H), 2.34 (s, 2H), 2.24 (d, J = 1.2 Hz, 3H), 1.35 (br s, 6H).

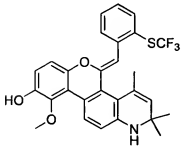
Example 51



(Z)-5-(2'-trifluoromethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 65, structure 1 of Scheme I, where R^1 = 2'-trifluoromethoxyphenyl)

[0211] This compound was prepared according to General Method 1 (Example 1) from 2-trifluoromethoxybenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.45 (d, J = 8.8 Hz, 1H), 8.34 (d, J = 8.3 Hz, 1H), 7.39 (m, 1H), 7.27-7.26 (m, 2H), 6.83 (d, J = 8.8 Hz, 1H), 6.79 (d, J = 8.3 Hz, 1H), 6.74 (d, J = 8.8 Hz, 1H), 5.94 (s, 1H), 5.49 (d, J = 1.0 Hz, 1H), 3.78 (s, 3H), 2.05 (d, J = 1.0 Hz, 3H), 1.29 (br s, 6H).

Example 52

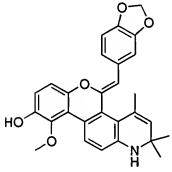


(Z)-5-(2'-trifluorothiobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 66, structure 1 of Scheme I, where R^1 = 2'-

trifluoromethylthiophenyl)

[0212] This compound was prepared according to General Method 1 (Example 1) from 2-trifluoromethylthiobenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.48 (d, J = 8.9 Hz, 1H), 8.36 (d, J = 8.6 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 6.80-6.76 (m, 2-overlapping signals, 2H), 6.72 (d, J = 8.9 Hz, 1H), 6.43 (s, 1H), 5.44 (s, 1H), 3.77 (s, 3H), 2.05 (s, 3H), 1.30 (br s, 6H).

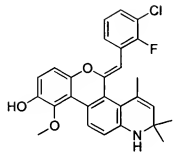
Example 53



(Z)-5-(3',4'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 67, structure 1 of Scheme I, where R^1 = 3',4'-methylenedioxyphenyl)

[0213] This compound was prepared according to General Method 1 (Example 1) from 3,4-methylenedioxybenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.26 (d, J = 8.9 Hz, 1H), 7.47 (d, J = 1.5 Hz, 1H), 7.00 (dd, J = 8.4, 1.4 Hz, 1H), 6.80-6.78 (m, 2H), 6.73-6.71 (m, 2H), 5.95 (s, 2H), 5.50-5.48 (m, 2H), 3.75 (s, 3H), 2.04 (d, J = 1.2 Hz, 3H), 1.30 (br s, 6H).

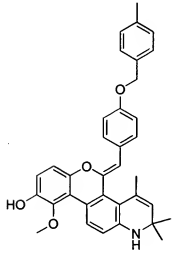
Example 54



(Z)-5-(3'-chloro-2'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 68, structure 1 of Scheme I, where R^1 =3'-chloro-2'-fluorophenyl)

[0214] This compound was prepared according to General Method 1 (Example 1) from 3-chloro-2-fluorobenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, J = 7.1 Hz, 1H), 8.21 (d, J = 7.4 Hz, 1H), 7.55 (m, 1H), 7.39 (m, 1H), 6.88 (m, 1H), 6.18 (s, 1H), 5.59 (s, 1H), 5.55 (s, 1H), 4.22 (s, 1H), 3.81 (s, 3H), 2.13 (s, 3H), 1.48 (br s, 6H).

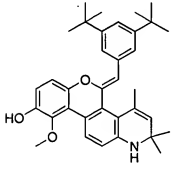
Example 55



(Z)-5-(4'-(4"-methylbenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 70, structure 1 of Scheme I, where R^1 = 4'-(4"-methylbenzyloxy)phenyl)

[0215] This compound was prepared according to General Method 1 (Example 1) from 4-(4'-methylbenzyloxy)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.26 (d, J = 8.6 Hz, 1H), 7.66 (d, J = 8.9 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H), 7.19 (d, J = 7.9 Hz, 2H), 6.97 (d, J = 8.9 Hz, 2H), 6.80 (d, J = 8.9 Hz, 1H), 6.73 (d, J = 8.6 Hz, 1H), 6.71 (d, J = 8.9 Hz, 1H), 5.50 (s, 2H), 5.04 (s, 2H), 3.75 (s, 3H), 2.34 (s, 3H), 2.05 (s, 3H), 1.30 (br s, 6H).

Example 56

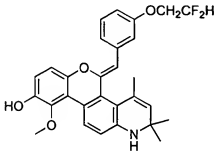


(Z)-5-(3',5'-di-tert-butylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 71, structure 1 of Scheme I, where R^1 = 3',5'-di-tert-butylphenyl)

[0216] This compound was prepared according to General Method 1 (Example 1) from 3,5-di-tertbutylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.9 Hz, 1H), 7.59-7.57 (m, 2H), 7.32 (app t, J = 1.2 Hz, 1H), 6.79-6.71 (m, 3H), 5.57 (s,

1H), 5.53 (d, J = 1.2 Hz, 1H), 3.76 (s, 3H), 2.09 (d, J = 1.0 Hz, 3H), 1.38-1.36 (m, 18H), 1.31 (br s, 6H).

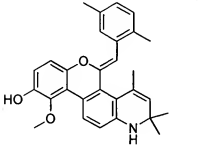
Example 57



(Z)-5-(3'-(2",2"-difluoroethoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 72, structure 1 of Scheme I, where R^1 = 3'-(2",2"-difluoroethoxy)phenyl

[0217] This compound was prepared according to General Method 1 (Example 1) from 3-(2',2'-difluoroethoxy)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.9 Hz, 1H), 7.42 (s, 1H), 7.28-7.25 (m, 2H), 6.87-6.71 (m, 4H), 6.19 (tt, J = 50.1, 2.9 Hz, 1H), 5.54 (s, 1H), 5.49 (s, 1H), 4.23 (t, J = 12.3 Hz, 2H), 3.74 (s, 3H), 2.04 (s, 3H), 1.29 (br s, 6H).

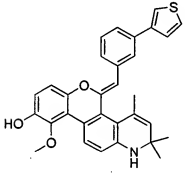
Example 58



(Z)-5-(2',5'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 73, structure 1 of Scheme I, where R^1 = 2',5'-dimethylphenyl

[0218] This compound was prepared according to General Method 1 (Example 1) from 2,5-dimethylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.30 (d, J = 8.6 Hz, 1H), 7.96 (s, 1H), 7.03 (d, J = 7.6 Hz, 1H), 6.92 (d, J = 7.3 Hz, 1H), 6.76 (d, J = 8.6 Hz, 1H), 6.72 (m, 2H), 5.83 (s, 1H), 5.50 (s, 1H), 3.77 (s, 3H), 2.36 (s, 3H), 2.21 (s, 3H), 2.11 (s, 3H), 1.31 (br s, 6H).

Example 59

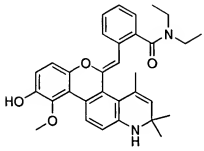


(Z)-5-(3'-(3"-thiophene)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 74, structure 1 of Scheme I, where R^1 = 3'-(3"-thiophene)phenyl)

[0219] This compound was prepared according to General Method 1 (Example 1) from 3-(3'-thiophene)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.30 (d, J = 8.9 Hz, 1H), 8.03 (s, 1H), 7.63-7.61 (m, 2H), 7.50-7.47 (m, 3H), 7.37 (t, J = 7.6 Hz, 1H), 6.83 (d, J = 8.9 Hz, 1H), 6.77 (d, J = 8.9 Hz, 1H), 6.75 (d, J = 9.8 Hz, 1H), 5.63 (s,

1H), 5.53 (s, 1H), 3.77 (s, 3H), 2.09 (s, 3H), 1.32 (br s, 6H).

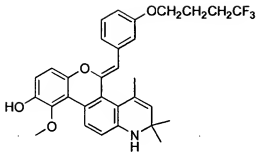
Example 60



(Z)-5-(2'-diethylaminocarbonylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 75, structure 1 of Scheme I, where R^1 =2'-di-ethylaminocarbonylphenyl)

[0220] General Method 2: N,N-diethyl-*o*-toluamide (230 mg, 1.2 mmol) was dissolved in tetrahydrofuran (1 mL) and added to a stirring solution of lithium diisopropylamide (1.6 mmol) in tetrahydrofuran (5 mL) at -78 °C. After 30 min, a solution of 9-hydroxy-10-methoxy-2,2,4-trimethyl-1,2-dihydro-5H-chromeno[3,4-f]quinoline-5-one (20 mg, 0.06 mmol) in tetrahydrofuran (1 mL) was added to a solution of the organolithium. The reaction was warmed to room temperature, then processed and carried forward as in the General Method 1. ^{1}H NMR (500 MHz, CD_3OD) δ 8.39-8.37 (m, 1H), 8.28 (d, J = 8.3 Hz, 1H), 7.47-7.33 (m, 2H), 7.27-7.23 (m, 1H), 7.16-7.12 (m, 1H), 6.75-6.72 (m, 1H), 6.69-6.67 (m, 1H), 5.70 (s, 1H), 5.48-5.46 (m, 1H), 3.72 (s, 3H), 3.50-3.48 (m, 1H), 3.41-3.39 (m, 1H), 3.18-3.00 (m, 2H), 2.07 (m, 3H), 1.40-0.9 (m, 12H).

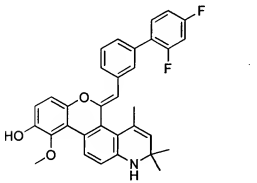
Example 61



(Z)-5-(3'-(4",4",4"-trifluorobutoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 76, structure 1 of Scheme I, where R^1 = 3'-(4",4",4"-trifluorobutoxy)phenyl)

[0221] This compound was prepared according to General Method 1 (Example 1) from 3-(4',4',4'-trifluorobutoxy)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.28 (d, J = 8.9 Hz, 1H), 7.39 (d, J = 1.2 Hz, 1H), 7.24-7.20 (m, 2H), 6.81-6.71 (m, 4H), 5.54 (s, 1H), 5.51 (d, J = 1.2 Hz, 1H), 4.09 (t, J = 6.1 Hz, 2H), 3.76 (s, 3H), 2.42-2.38 (m, 2H), 2.07-2.05 (m, 4H), 1.31 (br s, 6H).

Example 62

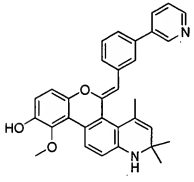


(Z)-5-(3'-(2",4"-difluorophenyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline (Compound 77, structure 1 of Scheme I, where R^1 =3-(2',4'-difluoro)biphenyl)

[0222] This compound was prepared according to General Method 1 (Example 1) from 3-(2',4'-difluorophenyl)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.28 (d, J = 8.9 Hz, 1H), 7.91 (s, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.55-7.48 (m, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.07-7.04 (m, 2H), 6.77 (d, J = 8.9 Hz, 1H), 6.75 (d, J = 8.6 Hz, 1H), 6.71 (d, J = 8.9 Hz, 1H), 5.62 (s, 1H), 5.51 (s, 1H), 3.75 (s, 3H), 2.07 (s, 3H), 1.30 (br s, 6H).

Example 63

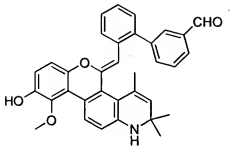


(Z)-5-(3'-(3"-pyridyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 78, structure 1 of Scheme I, where R^1 = 3-(3'-pyridyl)phenyl)

[0223] This compound was prepared according to General Method 1 (Example 1) from 3-(3'-pyridyl)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.82 (s, 1H), 8.57 (s, 1H), 8.30 (d, J = 8.6 Hz, 1H), 8.16 (d, J = 8.6 Hz, 1H), 8.05 (s, 1H), 7.77-7.74 (m, 1H), 7.61-7.56 (m, 1H), 7.48-7.45 (m, 2H), 6.81-6.73 (m, 3H), 5.67 (s, 1H), 5.53 (s,

1H), 3.76 (s, 3H), 2.09 (s, 3H), 1.32 (br s, 6H).

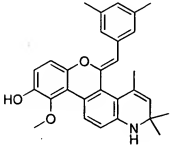
Example 64



(Z)-5-(2'-(3"-benzenecarbaldehyde)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 79, structure 1 of Scheme I, where R^1 = 2-(3'-benzenecarbaldehyde)phenyl

[0224] This compound was prepared according to General Method 1 (Example 1) from Compound 21 and 3-carbaldehydephenylboronic acid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.25 (d, J = 8.5 Hz, 1H), 7.87 (m, 1H), 7.77 (m, 1H), 7.55 (m, 2H), 7.48 (m, 1H), 7.29 (m, 1H), 7.25 (m, 1H), 6.82 (d, J = 8.5 Hz, 1H), 6.73 (d, J = 8.9 Hz, 1H). 6.67 (d, J = 8.9 Hz, 1H), 5.51 (s, 1H), 5.17 (d, J = 1.2 Hz, 1H), 3.81 (s, 3H), 1.91 (s, 3H), 1.29 (br s, 6H).

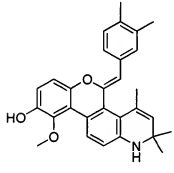
Example 65



(Z)-5-(3',5'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 80, structure 1 of Scheme I, where R^1 = 3',5'-dimethylphenyl)

[0225] This compound was prepared according to General Method 1 (Example 1) from 3,5-dimethylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.9 Hz, 1H), 7.59-7.57 (m, 2H), 7.32 (app t, J = 1.2 Hz, 1H), 6.79-6.71 (m, 3H), 5.57 (s, 1H), 5.53 (d, J = 1.2 Hz, 1H), 3.76 (s, 3H), 2.28 (s, 3H), 2.18 (s, 3H), 2.09 (s, 3H), 1.31 (br s, 6H).

Example 66

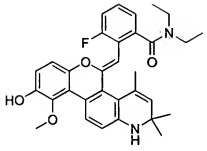


(Z)-5-(3',4'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 81, structure 1 of Scheme I, where R^1 = 3',4'-dimethylphenyl)

[0226] This compound was prepared according to General Method 1 (Example 1) from 3,4-dimethylbenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.26 (d, J = 8.9 Hz, 1H), 7.47 (d, J = 1.5 Hz, 1H), 7.00 (dd, J = 8.4, 1.4 Hz, 1H), 6.80-6.78 (m, 2H), 6.73-6.71 (m, 2H), 5.50-5.48 (m, 2H), 3.75 (s, 3H), 2.28 (s, 3H), 2.17 (s, 3H), 2.04 (s,

3H), 1.30 (br s, 6H).

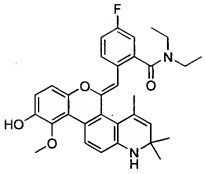
Example 67



(Z)-5-(2'-(diethylamino)carbonyl-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 82, structure 1 of Scheme I, where R^1 = 2'-(diethylamino)carbonyl-6'-fluorophenyl)

[0227] This compound was prepared according to General Method 2 (Example 65) from 6-fluoro-2-(N,N-diethyl)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.30 (d, J = 8.5 Hz, 1H), 7.40-7.35 (m, 2H), 7.25 (app t, J = 8.9 Hz, 1H), 7.18 (m, 1H), 7.06 (d, J = 7.6 Hz, 1H), 7.00 (dd, J = 7.6, 1.0 Hz, 1H), 6.77 (d, J = 8.5 Hz, 1H), 6.60 (d, J = 8.9 Hz, 1H), 6.42 (d, J = 8.5 Hz, 1H), 5.49 (s, 1H), 5.48 (d, J = 1.2 Hz, 1H), 3.73 (s, 3H), 3.50 (br s, 1H), 3.05 (br s, 1H), 2.85 (br s, 1H), 2.62 (br s, 1H), 2.17 (d, J = 1.2 Hz, 3H), 1.34-1.19 (m, 9H), 1.08 (t, J = 7.2 Hz, 3H).

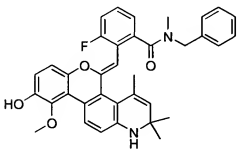
Example 68



(Z)-5-(2'-(diethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 83, structure 1 of Scheme I, where R^1 = 2'-(diethylamino)carbonyl-4'-fluorophenyl)

[0228] This compound was prepared according to General Method 2 (Example 1) from 4-fluoro-2-(N,N-diethyl)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.41-8.39 (m, 1H), 8.26 (d, J = 8.5 Hz, 1H), 7.22 (ddd, J = 11.6, 8.9, 2.9 Hz, 1H), 6.95 (dd, J = 8.5, 3.1 Hz, 1H), 6.75-6.68 (m, 3H), 5.51 (1H, s), 5.44 (d, J = 1.2 Hz, 1H), 3.72 (s, 3H), 3.44 (br s, 1H), 3.40 (br s, 1H), 3.05 (br s, 2H), 2.03 (d, J = 1.2 Hz, 3H), 1.28-1.19 (m, 12H).

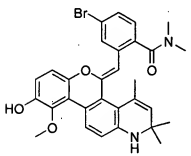
Example 69



(Z)-5-(2'-(methylbenzylamino)carbonyl-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 84, structure 1 of Scheme I, where R^1 = 2'-(methylbenzylamino)carbonyl-6'-fluorophenyl)

[0229] This compound was prepared according to General Method 2 (Example 65) from 6-fluoro-2-(N-methyl-N-benzyl)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.36 (d, J = 8.9 Hz, 0.3H), 8.24 (d, J = 8.9 Hz, 0.7H), 7.44-7.39 (m, 1H), 7.30-7.15 (m, 1H), 7.13-7.02 (m, 2H), 6.94-6.80 (m, 6H), 6.59 (d, J = 8.9 Hz, 0.3H), 6.51 (d, J = 8.9 Hz, 0.7H), 6.45 (d, J = 8.9 Hz, 0.3H), 6.36 (d, J = 8.9 Hz, 0.7H), 5.67 (s, 0.7H) 5.60 (s, 0.3H), 5.51 (d, J = 1.2 Hz, 1H), 5.22-5.20 (m, 2H), 3.80 (s, 3H), 2.21 (m, 3H), 1.48-1.10 (m, 6H).

Example 70

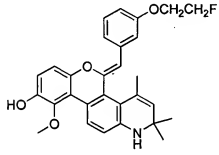


(Z)-5-(2'-(di-methylamino)carbonyl-5'-bromo-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 85, structure 1 of Scheme I, where R^1 = 2'-(di-methylamino)carbonyl-5'-bromophenyl)

[0230] This compound was prepared according to General Method 2 (Example 65) from 6-bromo-2-(N,N-dimethyl)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.63 (d,

J = 1.8 Hz, 1H), 8.34 (d, J = 8.9 Hz, 1H), 7.42 (dd, J = 8.1, 2.0 Hz, 1H), 7.11 (d, J = 8.2 Hz, 1H), 6.79-6.75 (m, 3H), 5.51 (d, J = 1.2 Hz, 1H), 5.49 (s, 1H), 3.77 (s, 3H), 3.03 (s, 3H), 2.79 (br s, 3H), 2.03 (d, J = 1.2 Hz, 3H), 1.29 (br s, 6H).

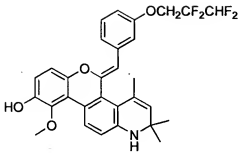
Example 71



(Z)-5-(3'-(2"-fluoroethoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 86, structure 1 of Scheme I, where R^1 = 3'-(2"-fluoroethoxy)phenyl)

[0231] This compound was prepared according to General Method 1 (Example 1) from 3-(2'-fluoroethoxy)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.9 Hz, 1H), 7.42 (s, 1H), 7.28-7.25 (m, 2H), 6.87-6.71 (m, 4H), 6.19 (tt, J = 50.1, 2.9 Hz, 1H), 5.54 (s, 1H), 5.49 (s, 1H), 4.23 (t, J = 12.3 Hz, 2H), 3.74 (s, 3H), 2.04 (s, 3H), 1.29 (br s, 6H).

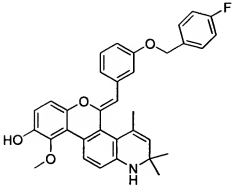
Example 72



(Z)-5-(3'-(2",2",3",3"-tetrafluoropropoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 87, structure 1 of Scheme I, where R^1 = 3'-(2",2",3",3"-tetrafluoropropoxy)phenyl)

[0232] This compound was prepared according to General Method 1 (Example 1) from 3-(2',2',3',3'-tetrafluoropropoxy)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD δ 8.28 (d, J = 8.6 Hz, 1H), 7.41 (s, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 6.80 (d, J = 8.9 Hz, 1H), 6.75 (d, J = 8.9 Hz, 1H), 6.72 (d, J = 8.9 Hz, 1H), 6.35 (tt, J = 50.1, 3.1 Hz, 1H), 5.55 (s, 1H), 5.51 (s, 1H), 4.47 (t, J = 12.5 Hz, 2H), 3.75 (s, 3H), 2.05 (s, 3H), 1.30 (br s, 6H).

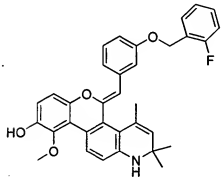
Example 73



(Z)-5-(3'-(4"-fluorobenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 88, structure 1 of Scheme I, where R^1 = 3'-(4"-fluorobenzyloxy)phenyl)

[0233] This compound was prepared according to General Method 1 (Example 1) from 3-(4'-fluorobenzyloxy)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.6 Hz, 1H), 7.50-7.42 (m, 3H), 7.28-7.19 (m, 2H), 7.11 (t, J = 8.9 Hz, 2H), 6.82 (d, J = 8.6 Hz, 1H), 6.75 (d, J = 8.6 Hz, 1H), 6.70 (s, 2H), 5.54 (s, 1H), 5.51 (s, 1H), 5.11 (s, 2H), 3.75 (s, 3H), 2.05 (s, 3H), 1.30 (br s, 6H).

Example 74

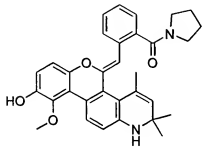


(Z)-5-(3'-(2"-fluorobenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 89, structure 1 of Scheme I, where R^1 = 3'-(2"-fluorobenzyloxy)phenyl)

[0234] This compound was prepared according to General Method 1 (Example 1) from 3-(2'-fluorobenzyloxy)benzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (d, J = 8.6 Hz, 1H), 7.56-7.49 (m, 2H), 7.38-7.31 (m, 1H), 7.24-7.12 (m, 4H), 6.83 (d, J = 8.5 Hz, 1H), 6.74 (d, J = 8.9 Hz, 1H), 6.72-6.69 (m, 2-overlapping signals, 2H), 5.54 (s,

1H), 5.50 (s, 1H), 5.18 (s, 2H), 3.75 (s, 3H), 2.05 (s, 3H), 1.30 (br s, 6H).

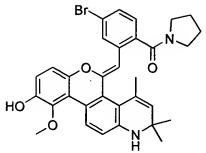
Example 75



(Z)-5-(2'-(pyrolidinecarbonylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 90, structure 1 of Scheme I, where R^1 = 2'-(pyrolidine)carbonylphenyl)

[0235] This compound was prepared according to General Method 2 (Example 65) from 2-(pyrolidine)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.42 (d, J = 7.9 Hz, 1H), 8.30 (d, J = 8.9 Hz, 1H), 7.47 (ddd, J = 9.0, 7.9, 1.5 Hz, 1H), 7.27 (ddd, J = 8.5, 7.3, 0.9 Hz, 1H), 7.20 (dd, J = 7.6, 1.5 Hz, 1H), 6.80-6.71 (m, 3H), 5.58 (s, 1H), 5.47 (d, J = 1.2 Hz, 1H), 3.74 (s, 3H), 3.50 (m, 2H), 3.10 (m, 2H), 2.05 (d, J = 1.2 Hz, 3H), 1.90 (m, 2H), 1.78 (m, 2H), 1.29 (br s, 6H).

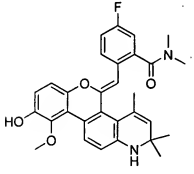
Example 76



(Z)-5-(2'-(pyrolidinecarbonyl-5'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 91, structure 1 of Scheme I, where R^1 = 5'-bromo-2'-(pyrolidine)carbonylphenyl)

[0236] This compound was prepared according to General Method 2 (Example 65) from 5-bromo-2-(pyrolidine)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.63 (d, J = 1.8 Hz, 1H), 8.34 (d, J = 8.9 Hz, 1H), 7.25 (dd, J = 8.0, 2.0 Hz, 1H), 7.25 (dd, J = 8.0, 2.0 Hz, 1H), 7.15 (d, J = 8.2 Hz, 1H), 6.79-6.74 (m, 3H), 5.54 (s, 1H), 5.48 (d, J = 1.2 Hz, 1H), 3.76 (s, 3H), 3.50 (m, 2H), 3.12 (m, 2H), 2.04 (d, J = 1.2 Hz, 3H), 1.91 (m, 2H), 1.82 (m, 2H), 1.28 (br s, 6H).

Example 77

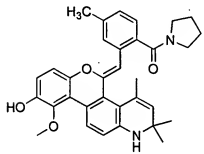


(Z)-5-(2'-(di-methylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 92, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(N,N-dimethylaminocarbonyl)phenyl)

[0237] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-(N,N-dimethyl)toluamide.^{1}H NMR (500 MHz, CD_3OD) δ 8.47 (dd, J = 8.9, 5.5 Hz, 1H), 8.46 (d, J = 8.9 Hz, 1H), 7.23 (ddd, J = 11.4, 8.7, 2.8 Hz, 1H), 6.95

(dd, J = 8.5, 2.7 Hz, 1H), 6.81 (d, J = 8.5 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 6.72 (d, J = 8.9 Hz, 1H), 5.49 (d, J = 1.2 Hz, 1H), 5.48 (1H, s), 3.79 (s, 3H), 3.03 (s, 3H), 2.80 (br s, 3H), 2.03 (d, J = 1.2 Hz, 3H), 1.29 (m, 6H).

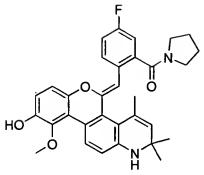
Example 78



(Z)-5-(2'-(pyrolidinecarbonyl-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 93, structure of Scheme I, where R^1 = 5'-methyl-2'-pyrolidine)carbonylphenyl)

[0238] This compound was prepared according to General Method 2 (Example 65) from 5-methyl-2-(pyrolidine)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.30 (d, J = 8.9 Hz, 1H), 8.25 (s, 1H), 7.11 (d, J = 0.9 Hz, 1H), 6.79-6.72 (m, 3H), 5.55 (s, 1H), 5.47 (d, J = 1.2 Hz, 1H), 3.75 (s, 3H), 3.49 (m, 2H), 3.10 (m, 2H), 2.44 (s, 3H), 2.05 (d, J = 1.2 Hz, 3H), 1.90 (m, 2H), 1.80 (m, 2H), 1.28 (br s, 6H).

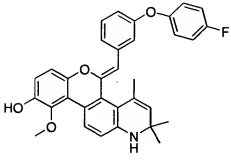
Example 79



(Z)-5-(2'-(pyrolidinecarbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 94, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(pyrolidine)carbonylphenyl)

[0239] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-(pyrolidine)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.45 (dd, J = 8.9, 5.5 Hz, 1H), 8.31-8.29 (m, 1H), 7.23 (ddd, J = 11.6, 8.9, 3.1 Hz, 1H), 7.02 (dd, J = 8.5, 3.1 Hz, 1H), 6.82-6.70 (m, 3H), 5.52 (1H, s), 5.48 (d, J = 1.2 Hz, 1H), 3.75 (s, 3H), 3.50 (m, 2H), 3.12 (m, 2H), 2.04 (d, J = 1.2 Hz, 3H), 1.89 (m, 2H), 1.80 (m, 2H), 1.28 (br s, 6H).

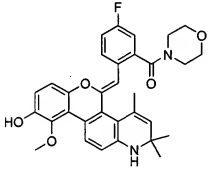
Example 80



(Z)-5-(3'-(4"-fluorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 95, structure 1 of Scheme I, where R^1 = 3'-(4"-fluorophenoxy)phenyl)

[0240] This compound was prepared according to General Method 1 (Example 1) from 3-(4'-fluorophenoxy)benzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.24 (d, J = 8.6 Hz, 1H), 7.56 (s, 1H), 7.28 (t, J = 7.9 Hz, 1H), 7.18-7.07 (m, 5H), 6.86 (d, J = 7.9 Hz, 1H), 6.72 (d, J = 8.9 Hz, 1H), 6.60 (d, J = 8.9 Hz, 1H), 6.22 (d, J = 8.8 Hz, 1H), 5.50 (s, 1H), 5.48 (s, 1H), 3.72 (s, 3H), 2.02 (s, 3H), 1.28 (br s, 6H).

Example 81

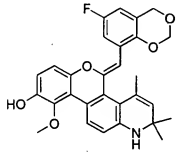


(Z)-5-(2'-(morpholinecarbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 96, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(morpholinecarbonyl)phenyl)

[0241] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-(morpholine)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.40-8.38 (m, 1H), 8.30 (d, J = 8.5 Hz, 1H), 7.25 (ddd, J = 11.4, 8.7, 2.7 Hz, 1H), 7.03 (dd, J = 8.5, 3.1 Hz, 1H), 6.79-6.74 (m, 1H), 6.71 (d, J = 8.9 Hz, 1H), 5.55 (1H, s), 5.50 (d, J =

1.2 Hz, 1H), 3.74 (s, 3H), 3.67-3.65 (m, 2H), 3.59-3.56 (m, 2H), 3.46-3.44 (m, 1H), 3.23-3.21 (m, 1H), 3.11-3.09 (m, 1H), 2.05 (d, J = 1.2 Hz, 3H), 1.32 (s, 3H), 1.28 (s, 3H).

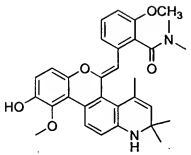
Example 82



(Z)-5-(5'-fluoro-benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 97, structure 1 of Scheme I, where R^1 = 5'-fluoro-benzo-(1,3-dioxan)phenyl)

[0242] This compound was prepared according to General Method 1 (Example 1) from 5-fluoro-benzo-(1,3-dioxan)benzyl chloride. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.9 Hz, 1H), 7.87 (dd, J = 10.7, 2.8 Hz, 1H), 6.83 (dd, J = 9.0, 8.2 Hz, 2H), 6.66 (d, J = 8.6 Hz, 1H), 6.54 (dd, J = 8.2, 3.1 Hz, 1H), 5.97 (s, 1H), 5.55 (s, 1H), 5.49 (s, 1H), 5.19 (s, 2H), 4.85 (s, 2H), 4.17 (s, 1H), 3.75 (s, 3H), 2.08 (s, 3H), 1.33 (br s, 6H).

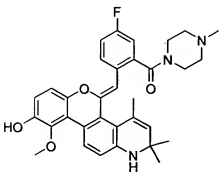
Example 83



(Z)-5-(2'-dimethylcarbonyl-3'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 98, structure 1 of Scheme I, where R^1 = 2'-(dimethylcarbonyl)-3'-methoxyphenyl)

[0243] This compound was prepared according to General Method 2 (Example 65) from 3-methoxy-2-(N,N-dimethyl)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.30 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 7.9 Hz, 1H), 7.42 (t, J = 8.2 Hz, 1H), 6.92 (d, J = 8.5 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 6.73 (d, J = 8.9 Hz, 1H), 5.49 (d, J = 1.2 Hz, 1H), 5.47 (s, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 3.04 (s, 3H), 2.80 (br s, 3H), 2.04 (s, 3H), 1.29 (s, 6H).

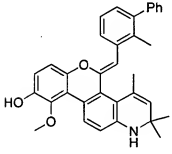
Example 84



(Z)-5-(2'-(4"-methylpiperazine)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 99, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(4"-methylpiperazine)carbonylphenyl)

[0244] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-(4'-methylpiperazine)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.40-8.38 (m, 1H), 8.31 (d, J = 8.9 Hz, 1H), 7.25 (ddd, J = 11.6, 8.9, 2.9 Hz, 1H), 7.02 (dd, J = 8.5, 2.7 Hz, 1H), 6.76 (dd, J = 8.9, 3.1 Hz, 1H), 6.70 (d, J = 8.7 Hz, 1H), 5.51 (s, 1H), 5.50 (m, 1H) 3.75 (s, 3H), 3.63-3.61 (m, 1H), 3.30 (m, 2H, obscured by solvent), 3.15-3.05 (m, 2H), 2.43-2.41 (m, 2H), 2.21-2.19 (m, 4H), 2.04 (d, J = 1.5 Hz, 3H), 1.31-1.28 (m, 6H).

Example 85

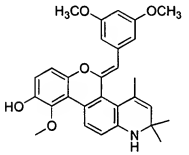


(Z)-5-(2'-methyl-3'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 100, structure 1 of Scheme I, where R^1 = 2'-methyl-3'-biphenyl)

[0245] This compound was prepared according to General Method 1 (Example 1) from 2-methyl-3-phenylbenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J =

8.6 Hz, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.38 (m, 2H), 7.33-7.29 (m, 4H), 7.10 (m, 1H), 6.81 (m, 2H), 6.68 (m, 1H), 5.91 (s, 1H), 5.54 (s, 1H), 5,49 (s, 1H), 4.18 (s, 1H), 3.80 (s, 3H), 2.18 (s, 3H), 2.15 (s, 3H), 1.35 (br s, 6H).

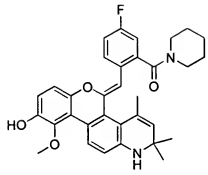
Example 86



(Z)-5-(3',5'-di-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 101, structure 1 of Scheme I, where R^1 = 3',5'-dimethoxyphenyl)

[0246] This compound was prepared according to General Method 1 (Example 1) from 3,5-dimethoxybenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.9 Hz, 1H), 6.97 (s, 1H), 6.86 (d, J = 8.6 Hz, 1H), 6.81 (d, J= 8.6 Hz, 1H), 6.67 (d, J = 8.7 Hz, 1H), 6.37 (s, 1H), 5.59 (s, 1H), 5.55 (s, 1H), 5.51 (s, 1H), 3.85 (s, 6H), 3.78 (s, 3H), 2.10 (s, 3H), 1.35 (br s, 6H).

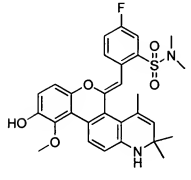
Example 87



(Z)-5-(2'-(piperidineamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 102, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(piperdinecarbonyl)phenyl)

[0247] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-piperidinetoluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.41-8.39 (m, 1H), 8.29 (d, J = 8.5 Hz, 1H), 7.25 (ddd, J = 11.6, 8.7, 2.7 Hz, 1H), 6.97 (dd, J = 8.5, 2.7 Hz, 1H), 6.75 (d, J = 8.9 Hz, 1H), 6.69 (d, J = 8.5 Hz, 1H), 5.52 (1H, s), 5.47 (d, J = 0.6 Hz, 1H), 3.73 (s, 3H), 3.69-3.67 (m, 1H), 3.53-3.52 (m, 1H), 3.14-3.08 (m, 2H), 2.04 (s, 3H), 1.57-1.54 (m, 4H) 1.30-1.28 (m, 8H).

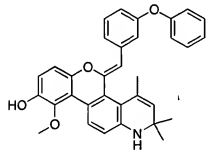
Example 88



(Z)-5-(2'-dimethylaminosulphonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 103, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(dimethylaminosulphonyl)phenyl

[0248] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-(N,N-dimethyl)benzenesulfonamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.36 (dd, J = 8.9, 5.5 Hz, 1H), 8.29 (d, J = 8.5 Hz, 1H), 7.63 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (ddd, J = 11.1, 8.4, 2.9 Hz, 1H), 6.78 (d, J = 8.5 Hz, 1H), 6.63 (d, J = 8.9 Hz, 1H), 6.62 (d, J = 8.9 Hz, 1H), 6.43 (s, 1H), 5.49 (d, J = 1.5 Hz, 1H), 3.73 (s, 3H), 2.48 (s, 6H), 2.08 (d, J = 1.2 Hz, 3H), 1.30 (br s, 6H).

Example 89

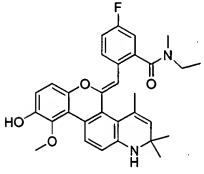


(Z)-5-(3'-(phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 104, structure 1 of Scheme I, where R^1 = 3'-phenoxyphenyl)

[0249] This compound was prepared according to General Method 1 (Example 1) from 3-phenoxybenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.25 (d, J = 8.9 Hz, 1H), 7.60 (s, 1H), 7.42 (t, J = 1.2 Hz, 2H), 7.29 (t, J = 1.5 Hz, 1H), 7.20 (t, J = 1.2 Hz,

1H), 7.16 (d, J = 7.6 Hz, 1H), 7.08-7.06 (m, 2-overlapping signals, 2H), 6.87 (d, J = 7.6 Hz, 1H), 6.73 (d, J = 8.6 Hz, 1H), 6.59 (d, J = 8.6 Hz, 1H), 6.22 (d, J = 8.9 Hz, 1H), 5.52 (s, 1H), 5.50 (s, 1H), 3.73 (s, 3H), 2.03 (s, 3H), 1.29 (br s, 6H).

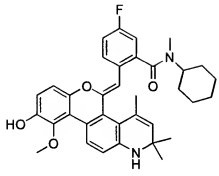
Example 90



(Z)-5-(2'-(ethylmethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 105, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(ethylmethylamino)carbonyl)phenyl)

[0250] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-(N-ethyl-N-methyl)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.46 (dd, J = 8.9, 5.6 Hz, 1H), 8.30 (m, 1H, rotamers), 7.23 (ddd, J = 11.4, 8.7, 2.7 Hz, 1H), 6.99-6.95 (m, 1H, rotamers), 6.81-6.70 (m, 3H, rotamers), 5.52-5.47 (m, 2H, rotamers), 3.75-3.73 (m, 3H), 3.13-3.11 (m, 2H), 2.99 (s, 2H, rotamers), 2.72 (1H, s, rotamers), 2.04-2.02 (m, 3H), 1.27 (br s, 6H), 1.18-1.14 (m, 3H).

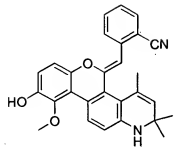
Example 91



(Z)-5-(2'-(cyclohexylmethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 106, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(cyclohexylmethylamino)carbonyl)phenyl)

[0251] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-(N-cyclohexyl-N-methyl)toluamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.37-8.34 (m, 1H), 8.30-8.28 (m, 1H), 7.26-7.24 (m, 1H), 6.97-6.95 (m, 1H), 6.77-6.75 (m, 1H), 6.70-6.68 (m, 1H), 5.52-5.42 (m, 2H), 4.31-4.29 (m, 1H), 3.74-3.73 (m, 3H), 3.08-3.06 (m, 1H), 2.85-2.83 (m, 2H), 2.61-2.59 (m, 1H), 2.06-2.03 (m, 3H), 1.66-1.00 (m, 15H).

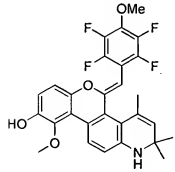
Example 92



(Z)-5-(2'-cyanobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 107, structure 1 of Scheme I, where R^1 = 2'-cyanophenyl)

[0252] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-benzonitrile. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 8.5 Hz, 1H), 7.60 (m, 2H), 7.25 (m, 1H), 6.85 (d, J = 8.6 Hz, 1H), 6.74 (d, J =8.6 Hz, 1H), 6.13 (s, 1H), 5.60 (m, 2H), 3.81 (s, 3H), 2.12 (s, 3H), 1.37 (br s, 6H).

Example 93

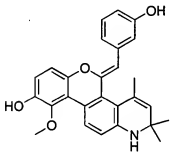


(Z)-5-(2',3',5',6'-tetrafluoro-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 108, structure 1 of

Scheme I, where R^1 = 2',3',5',6'-tetrafluoro-4'-methoxyphenyl)

[0253] This compound was prepared according to General Method 1 (Example 1) from 2,3,5,6-tetrafluoro-4-methoxybenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.35 (d, J = 8.6 Hz, 1H), 6.80 (d, J = 8.6 Hz, 1H), 6.67 (d, J = 8.9 Hz, 1H), 6.57 (d, J = 8.9 Hz, 1H), 5.51 (s, 1H), 5.42 (s, 1H), 4.07 (s, 3H), 3.77 (s, 3H), 2.14 (s, 3H), 1.29 (br s, 6H).

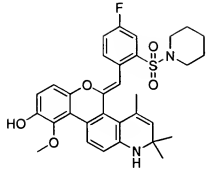
Example 94



(Z)-5-(3'-hydroxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 109, structure 1 of Scheme I, where R^1 = 3'-hydroxyphenyl)

[0254] This compound was prepared according to General Method 1 (Example 1) from 3-trimethylsiloxybenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.26 (d, J = 8.9 Hz, 1H), 7.33-7.32 (m, 1H), 7.12 (t, J = 7.9 Hz, 1H), 7.07-7.04 (m, 1H), 6.88 (d, J = 8.6 Hz, 1H), 6.73 (d, J = 8.6 Hz, 1H), 6.71 (d, J = 8.9 Hz, 1H), 6.62 (d, J = 8.6 Hz, 1H), 5.50 (s, 1H), 5.48 (s, 1H), 3.75 (s, 3H), 2.05 (s, 3H), 1.30 (br s, 6H).

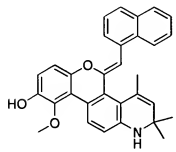
Example 95



(Z)-5-(2'-(piperidinesulphonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 110, structure 1 of Scheme I, where R^1 = 4'-fluoro-2'-(piperidinesulphonyl)phenyl)

[0255] This compound was prepared according to General Method 2 (Example 65) from 4-fluoro-2-(piperidine)benzenesulfonamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.30 (d, J = 8.5 Hz, 1H), 8.26 (dd, J = 8.9, 5.5 Hz, 1H), 7.64 (dd, J = 8.9, 3.1 Hz, 1H), 7.46 (ddd, J = 11.3, 8.2, 3.1 Hz, 1H), 6.79 (d, J = 8.9 Hz, 1H), 6.64 (d, J = 8.9 Hz, 1H), 6.59 (d, J = 8.9 Hz, 1H), 6.35 (s, 1H), 5.50 (d, J = 1.2 Hz, 1H), 3.73 (s, 3H), 2.82-2.80 (m, 4H), 2.09 (d, J = 1.2 Hz, 3H), 1.30 (br s, 6H), 1.28-1.17 (m, 6H).

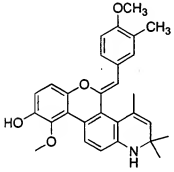
Example 96



(Z)-5-(2'-napthylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 111, structure 1 of Scheme I, where R^1 = 2'-napthyl)

[0256] This compound was prepared according to General Method 1 (Example 1) from 2-napthylbromide. ^{1}H NMR (500MHz, $CDCl_3$) δ 8.27 (d, J = 7.3 Hz, 1H), 8.20 (d, J = 8.5 Hz, 1H), 7.99-8.00 (m, 1H), 7.84-7.86 (m, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.56 (t, J = 7.9 Hz, 1H), 7.45-7.46 (m, 1H), 6.76-6.78 (m, 4H), 6.72 (d, J = 8.5 Hz, 1H), 6.39 (s, 1H), 5.54 (s, 1H), 4.21 (br s, 1H), 3.80 (s, 3H), 2.19 (d, J = 1.2 Hz, 3H), 1.39 (s, 6H).

Example 97

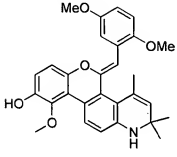


(Z)-5-(3'-methyl-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2-cyclohexyl-4-methyl-5H-chromeno[3,4-f]quinoline (Compound 112, structure 1 of Scheme I, where R^1 = 4'-methoxy-3'-methylphenyl)

[0257] This compound was prepared according to General Method 1 (Example 1) from 4-methoxy-3-methylbenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 8.6 Hz, 1H), 7.63 (m, 1H), 7.54 (m, 1H,), 6.89 (d, J = 7.9 Hz, 1H), 6.83 (d, J = 8.6 Hz, 1H), 6.66 (d, J = 8.6 Hz, 1H), 6.14 (s, 1H), 5.56 (s, 1H), 5.50 (m, 2H), 4.16 (s, 1H), 3.85

(s, 3H), 3.81 (s, 3H), 2.25 (s, 3H), 2.09 (s, 3H), 1.35 (br s, 6H).

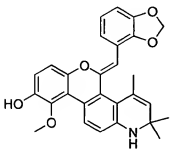
Example 98



(Z)-5-(2',5'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2-cyclohexyl-4-methyl-5H-chromeno[3,4-f]quinoline (Compound 113, structure 1 of Scheme I, where R^1 = 2',5'-dimethoxyphenyl)

[0258] This compound was prepared according to General Method 1 (Example 1) from 2,5-dimethoxybenzyl bromide. ^{1}H NMR (400 MHz, CD_3Cl) δ 8.13 (d, J = 8.6 Hz, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.30 (s, 1H), 6.88 (m, 3H), 6.67 (d, J = 8.6 Hz, 1H), 6.07 (s, 1H,), 5.56 (s, 1H), 5.51 (m, 2H), 4.24 (s, 1H), 3.87 (s, 3H), 3.77 (s, 3H), 3.75 (s, 3H), 2.12 (s, 3H), 1.35 (br s, 6H).

Example 99

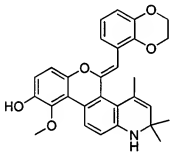


(Z)-5-(2',3'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline (Compound 114, structure 1 of Scheme I, where R^1 = 2',3'-methylenedioxyphenyl)

[0259] This compound was prepared according to General Method 1 (Example 1) from 2,3-methylenedioxybenzyl bromide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.72 (m, 2H), 6.84 (t, J = 7.9 Hz, 1H), 6.70 (d, J = 8.6 Hz, 2H), 5.92 (s, 1H), 5.88 (s, 1H), 5.55 (m, 2H), 5.29 (s, 2H), 3.79 (s, 3H), 2.11 (s, 3H), 1.34 (br s, 6H).

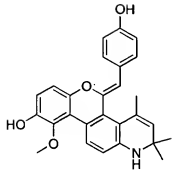
Example 100



(Z)-5-(2',3'-ethylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 115, structure 1 of Scheme I, where R^1 = 2',3'-ethylenedioxyphenyl)

[0260] This compound was prepared according to General Method 1 (Example 1) from 2,3-ethylenedioxybenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.27 (m, 2H), 8.04 (s, 1H), 6.88 (m, 1H), 6.72 (m, 2H), 5.88 (s, 1H), 5.45 (m, 2H), 3.73 (s, 3H), 3.68 (m, 4H), 2.02 (s, 3H), 1.26 (br s, 6H).

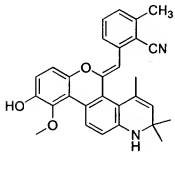
Example 101



(Z)-5-(4'-hydroxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 116, structure 1 of Scheme I, where R^1 = 4'-hydroxyphenyl)

[0261] This compound was prepared according to General Method 1 (Example 1) from 4-trimethylsiloxybenzyl bromide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.22 (d, J = 8.6 Hz, 1H), 7.56-7.54 (m, 2-overlapping signals, 2H), 6.78-6.74 (m, 3H), 6.70-6.67 (m, 2H), 5.47 (s, 1H), 5.44 (s, 1H), 3.72 (s, 3H), 2.02 (s, 3H), 1.28 (br s, 6H).

Example 102

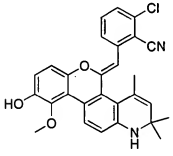


(Z)-5-(2'-cyano-3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 117, structure 1 of Scheme I, where

R^1 = 2'-cyano-3'-methylphenyl)

[0262] This compound was prepared according to General Method 2 (Example 65) from 2,6-dimethyl-benzonitrile. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.1 Hz, 1H), 8.20 (d, J = 8.6 Hz, 1H), 7.47 (t, J = 7.9 Hz, 1H), 7.11 (d, J = 7.9 Hz, 1H), 6.88 (d, J = 8.6 Hz, 1H), 6.72 (d, J = 8.6 Hz, 1H), 6.14 (s, 1H), 5.59 (m, 2H), 4.24 (s, 1H), 3.81 (s, 3H), 2.53 (s, 3H), 2.12 (s, 3H), 1.37 (br s, 6H).

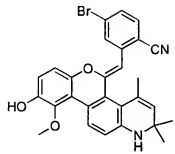
Example 103



(Z)-5-(3'-chloro-2'-cyanobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 118, structure 1 of Scheme I, where R^1 = 3'-chloro-2'-cyanophenyl)

[0263] This compound was prepared according to General Method 2 (Example 65) from 2-chloro-6-methylbenzonitrile. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.6 Hz, 1H), 8.23 (d, J = 7.9 Hz, 1H), 7.49 (t, J = 7.9 Hz, 1H), 7.29 (s, 1H), 6.88 (d, J = 8.6 Hz, 1H), 6.76 (d, J = 8.6 Hz, 1H), 6.12 (s, 1H), 5.59 (m, 2H), 4.26 (s, 1H), 3.81 (s, 3H), 2.11 (s, 3H), 1.37 (br s, 6H).

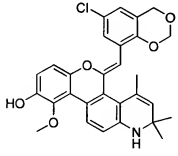
Example 104



(Z)-5-(5'-bromo-2'-cyano-benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 119, structure 1 of Scheme I, where R^1 = 5'-bromo-2'-cyanophenyl)

[0264] This compound was prepared according to General Method 2 (Example 65) from 4-bromo-2-methylbenzonitrile. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (m, 1H), 8.24 (d, J = 8.2 Hz, 1H), 7.45 (m, 1H), 7.36 (m, 1H), 6.93 (m, 2H), 6.75 (m, 1H), 6.07 (s, 1H), 5.60 (m, 2H), 4.22 (s, 1H), 3.81 (s, 3H), 2.10 (s, 3H), 1.36 (br s, 6H).

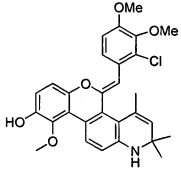
Example 105



(Z)-5-(5'-chloro-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 120, structure 1 of Scheme I, where R^1 = 5'-chloro-benzo-(1,3-dioxan)phenyl

[0265] This compound was prepared according to General Method 1 (Example 1) from 5-chloro-benzo-(1,3-dioxan)benzyl chloride. ^{1}H NMR (400 MHz, CD_3OD) δ 8.27 (d, J = 8.8 Hz, 1H), 8.04 (d, J = 2.5 Hz), 1H), 6.85 (d, J = 2.4 Hz, 1H), 6.74-6.71 (m, 3H), 5.89 (s, 1H), 5.45 (s, 1H), 5.19 (s, 2H), 4.81 (s, 2H), 3.73 (s, 3H), 2.03 (s, 3H), 1.27 (br s, 6H).

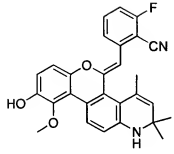
Example 106



(Z)-5-(2'-chloro-3',4'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 121, structure 1 of Scheme I, where R^1 = 2'-chloro-3',4'-dimethoxyphenyl)

[0266] This compound was prepared according to General Method 1 (Example 1) from 2-chloro-3,4-dimethoxybenzyl bromide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.6 Hz, 1H), 8.21 (d, J = 7.9 Hz, 1H), 7.49 (t, J = 7.9 Hz, 1H), 7.11 (d, J = 7.9 Hz, 1H), 6.88 (d, J = 8.6 Hz, 1H), 6.72 (d, J = 8.6 Hz, 1H), 6.14 (s, 1H), 5.88 (s, 1H), 5.59 (s, 1H), 3.96 (s, 3H), 3.81 (s, 3H), 3.55 (s, 3H), 2.12 (s, 3H), 1.37 (br s, 6H).

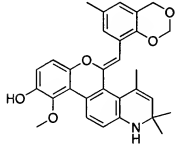
Example 107



(Z)-5-(2'-cyano-3'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 122, structure 1 of Scheme I, where R^1 = 2'-cyano-3'-fluorophenyl)

[0267] This compound was prepared according to General Method 2 (Example 65) from 2-fluoro-6-methylbenzonitrile. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (m, 2H), 7.55 (m, 1H), 6.98 (m, 1H), 6.88 (m, 2H), 6.72 (m, 2H), 6.08 (s, 1H), 5.61 (s, 1H), 3.81 (s, 3H), 2.11 (s, 3H), 1.37 (br s, 6H).

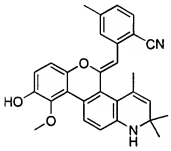
Example 108



(Z)-5-(5'-methyl-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 123, structure 1 of Scheme I, where R^1 = 5'-methyl-benzo-(1,3-dioxan)phenyl)

[0268] This compound was prepared according to General Method 1 (Example 1) from 5-methyl-benzo-(1,3-dioxan)benzyl chloride. ^{1}H NMR (400 MHz, CD_3OD) δ 8.23 (d, J = 8.7 Hz, 1H), 7.85 (s, 1H), 6.72-6.64 (m, 4H), 5.89 (s, 1H), 5.45 (s, 1H), 5.15 (s, 2H), 4.79 (s, 2H), 3.73 (s, 3H), 2.28 (s, 3H), 2.05 (s, 3H), 1.26 (br s, 6H).

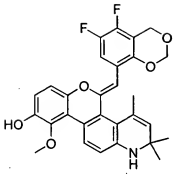
Example 109



(Z)-5-(2'-cyano-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 124, structure 1 of Scheme I, where R^1 = 2'-cyano-5'-methylphenyl)

[0269] This compound was prepared according to General Method 2 (Example 65) from 2,4-dimethylbenzonitrile. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (m, 1H), 7.67 (m, 2H), 7.54 (m, 1H), 6.88 (m, 1H), 6.66 (m, 2H), 5.60 (m, 2H), 5.53 (s, 1H), 4.22 (s, 1H), 3.81 (s, 3H), 2.56 (s, 3H), 2.07 (s, 3H), 1.36 (br s, 6H).

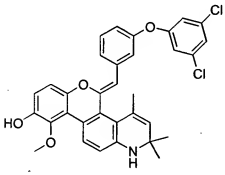
Example 110



(Z)-5-(4',5'-difluoro-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 125, structure 1 of Scheme I, where R^1 = 4',5'-difluoro-benzo-(1,3-dioxan)phenyl

[0270] This compound was prepared according to General Method 1 (Example 1) from 5-methyl-benzo-(1,3-dioxan)benzyl chloride. ^{1}H NMR (400 MHz, CD_3Cl) δ 8.23 (d, J = 8.7 Hz, 1H), 7.95 (m, 1H), 6.72-6.64 (m, 4H), 5.89 (s, 1H), 5.55 (s, 1H), 5.15 (s, 2H), 4.86 (s, 2H), 3.73 (s, 3H), 2.03 (s, 3H), 1.26 (br s, 6H).

Example 111

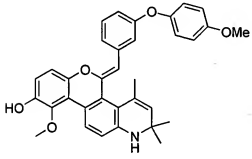


(Z)-5-(3'-(3",5"-dichlophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 126, structure 1 of Scheme I,

where R^1 = 3'-(3",5"-dichlorophenoxy)phenyl)

[0271] This compound was prepared according to General Method 1 (Example 1) from 3-(3',5'-dichlorophenoxy)benzyl bromide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.25 (d, J = 8.6 Hz, 1H), 7.60 (s, 1H), 7.34 (t, J = 7.9 Hz, 1H), 7.25 (d, J = 7.7 Hz, 1H), 7.21 (t, J = 1.6 Hz, 1H), 6.98 (s, 2H), 6.89 (dd, J = 7.8, 1.7 Hz, 1H), 6.72 (d, J = 8.7 Hz, 1H), 6.63 (d, J = 8.9 Hz, 1H), 6.37 (d, J = 8.9 Hz, 1H), 5.55 (s, 1H), 5.47 (s, 1H), 3.72 (s, 3H), 2.02 (s, 3H), 1.26 (br s, 6H).

Example 112

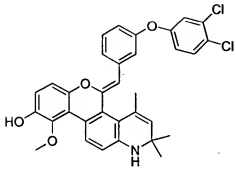


(Z)-5-(3'-(4"-methoxy)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 127, structure 1 of Scheme I, where R^1 = 3'-(4"-methoxy)phenoxyphenyl)

[0272] This compound was prepared according to General Method 1 (Example 1) from 3-(4'-methoxyphenoxy)benzyl bromide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.6 Hz, 1H), 7.57 (s, 1H), 7.25-7.23 (m, 1H), 7.07-7.05 (m, 2-overlapping signals, 2H), 6.95-6.92 (m, 2-overlapping signals, 2H), 6.85 (d, J = 7.9 Hz, 1H), 6.73 (d, J = 8.7 Hz, 1H), 6.65 (d, J = 8.6 Hz, 1H), 6.43 (d, J = 8.7 Hz, 1H), 5.56 (s, 1H), 5.53 (s, 1H),

5.51 (s, 1H), 4.17 (s, 1H), 3.85 (s, 3H), 3.76 (s, 3H), 2.08 (s, 3H), 1.34 (br s, 6H).

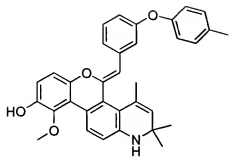
Example 113



(Z)-5-(3'-(3",4"-dichlorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 128, structure 1 of Scheme I, where R^1 = 3'-(3",4"-dichlorophenoxy)phenyl)

[0273] This compound was prepared according to General Method 1 (Example 1) from 3-(3',4'-dichlorophenoxy)benzyl bromide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.6 Hz, 1H), 7.57 (s, 1H), 7.43-7.39 (m, 2H), 7.33 (t, J = 7.9 Hz, 1H), 7.16 (d, J = 2.7 Hz, 1H), 6.93 (dd, J = 8.8, 2.8 Hz, 1H), 6.89 (d, J = 7.8 Hz, 1H), 6.80 (d, J = 8.8 Hz, 1H), 6.67 (d, J = 8.6 Hz, 1H), 6.56 (d, J = 8.7 Hz, 1H) 5.58 (s, 1H), 5.56 (s, 1H), 5.51 (s, 1H), 4.19 (s, 1H), 3.77 (s, 3H), 2.08 (s, 3H), 1.35 (br s, 6H).

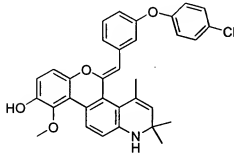
Example 114



(Z)-5-(3'-(4"-methyl)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 129, structure 1 of Scheme I, where R^1 = 3'-(4"-methyl)phenoxyphenyl)

[0274] This compound was prepared according to General Method 1 (Example 1) from 3-(4'-methyl)phenoxybenzyl bromide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.6 Hz, 1H), 7.59 (s, 1H), 7.31-7.27 (m, 2H), 7.20-7.18 (m, 2-overlapping signals, 2H), 7.01-6.99 (m, 2-overlapping signals, 2H), 6.89-6.87 (m, 1H), 6.72 (d, J = 8.9 Hz, 1H), 6.65 (d, J = 8.6 Hz, 1H), 6.43 (d, J = 8.9 Hz, 1H), 5.56 (s, 1H), 5.55 (s, 1H), 5.51 (s, 1H), 4.17 (s, 1H), 3.75 (s, 3H), 2.39 (s, 3H), 2.08 (s, 3H), 1.34 (br s, 6H).

Example 115

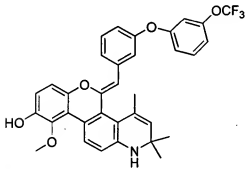


(Z)-5-(3'-(4"-chloro)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-

trimethyl-5H-chromeno[3,4-f]quinoline (Compound 130, structure 1 of Scheme I, where R^1 = 3'-(4"-chloro)phenoxyphenyl)

[0275] This compound was prepared according to General Method 1 (Example 1) from 3-(4'-chloro)phenoxybenzyl bromide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.6 Hz, 1H), 7.59 (s, 1H), 7.36-7.28 (m, 4H), 7.04-7.01 (m, 2-overlapping signals, 2H), 6.89 (d, J = 8.7 Hz, 1H), 6.79 (d, J = 8.9 Hz, 1H), 6.66 (d, J = 8.6 Hz, 1H), 6.47 (d, J = 8.9 Hz, 1H), 5.57 (s, two overlapping signals, 2H), 5.51 (s, 1H), 4.15 (s, 1H), 3.77 (s, 3H), 2.08 (s, 3H), 1.34 (br s, 6H).

Example 116

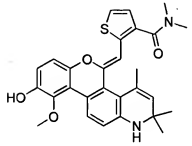


(Z)-5-(3'-(3"-trifluoromethoxy)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4- f]quinoline (Compound 131, structure 1 of Scheme I, where R^1 = 3'-(3"-trifluoromethoxy)phenoxyphenyl)

[0276] This compound was prepared according to General Method 1 (Example 1) from 3-(3'-trifluoromethoxy)phenoxybenzyl bromide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.6 Hz, 1H), 7.58 (t, J = 1.7 Hz, 1H), 7.49-7.32 (m, 5H), 7.23 (d, J = 8.2 Hz, 1H), 6.90 (d, J = 7.9 Hz, 1H), 6.75 (d, J = 8.9 Hz, 1H), 6.67 (d, J = 8.6 Hz, 1H), 6.55 (d,

J = 8.7 Hz, 1H), 5.59 (s, 1H), 5.56 (s, 1H), 5.51 (s, 1H), 4.19 (s, 1H), 3.76 (s, 3H), 2.09 (s, 3H), 1.34 (br s, 6H).

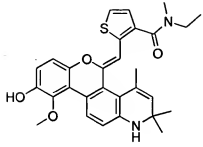
Example 117



(Z)-5-(2'-(3'-(dimethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 132, structure 1 of Scheme I, where R^1 = 2'-(3'-dimethylaminocarbonyl)thiophenyl)

[0277] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(N,N-dimethyl)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, *J* = 8.8 Hz, 1H), 7.40 (d, *J* = 5.4 Hz, 1H), 6.98 (dd, *J* = 5.4, 1.0 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.77-6.74 (m, 2H), 5.87 (s, 1H), 5.51 (d, *J* = 1.0 Hz, 1H), 3.76 (s, 3H), 3.05 (s, 3H), 2.89 (s, 3H), 2.00 (s, 3H), 1.29 (br s, 6H).

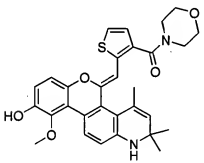
Example 118



(Z)-5-(2'-(3'-(ethylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 134, structure 1 of Scheme I, where R^1 = 2'-(3'-ethylmethylaminocarbonyl)thiophenyl)

[0278] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(N-ethyl-N-methyl)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.33 (d, J = 8.3 Hz, 1H), 7.40 (d, J = 4.9 Hz, 1H), 6.99-6.94 (m, 2H), 6.76 (d, J = 3.4 Hz, 1H), 6.75 (d, J = 3.4 Hz, 1H), 5.88 (d, J = 8.3 Hz, 1H) 5.51-5.48 (m, 2H), 3.76 (s, 3H), 3.53-3.51 (m, 1H), 3.24 (q, J = 6.6 Hz, 1H), 3.02 (s, 1.4 H), 2.87 (s, 1.6 H), 2.01 (m, 3H, rotamers), 1.28 (br s 6H), 1.22 (t, J = 7.1 Hz, 1.4 H), 1.03 (t, J = 7.1 Hz, 1.6H).

Example 119

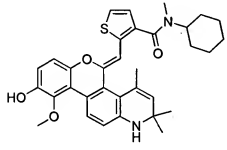


(Z)-5-(2'-(3'-(morpholinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 135, structure 1 of Scheme I, where R^1 = 2'-(3'-morpholinocarbonyl)thiophenyl)

[0279] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(morpholine)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, J = 8.8 Hz, 1H), 7.41 (d, J = 5.4 Hz, 1H), 7.00 (dd, J = 5.4, 1H), 6.95 (d, J = 8.8 Hz,

1H), 6.77 (d, J = 8.3 Hz, 1H), 6.75 (d, J = 8.8 Hz, 1H), 5.95 (s, 1H), 5.51 (d, J = 1.5 Hz, 1H), 3.76 (s, 3H), 3.70-3.68 (m, 3H), 3.52-3.50 (m, 3H), 3.34-3.30 (m, 2H, partially obscured by solvent), 2.02 (d, J = 1.0 Hz, 3H), 1.30 (br s, 6H).

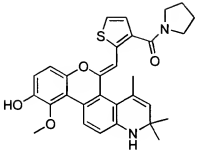
Example 120



(Z)-5-(2'-(3'-cyclohexylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 136, structure 1 of Scheme I, where R^1 = 3'-(cyclohexylmethylamino)carbonylthiophenyl)

[0280] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(N,N-dimethyl)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.33 (d, J = 8.8 Hz, 1H), 7.42 (app t, J = 6.1 Hz, 1H), 6.99-6.94 (m, 2H), 6.76-6.75 (m, 2H), 5.85 (s, 1H), 5.45 (s, 1H), 4.39-4.37 (m, 1H), 3.75 (s, 3H), 3.41-3.38 (m, 1.5 H), 2.95 (s, 1.5 H), 2.75 (s, 1.5 H), 2.01-1.99 (m, 3H, rotamers), 1.87-1.01 (m, 16H).

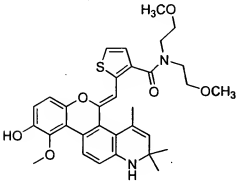
Example 121



(Z)-5-(2'-(3'-(pyrrolidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 137, structure 1 of Scheme I, where R^1 = 2'-(3'-pyrolidinocarbonylthiophenyl)

[0281] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(pyrolidine)thiophenamide. ^{1}H NMR (400 MHz, CD_3OD) δ 8.34 (d, J = 8.8 Hz, 1H), 7.38 (d, J = 5.4 Hz, 1H), 7.01 (d, J = 5.2 Hz, 1H), 6.95 (d, J = 8.7 Hz, 1H), 6.77-6.74 (m, 2-overlapping signals, 2H), 5.95 (s, 1H), 5.48 (s, 1H), 3.76 (s, 3H), 3.52 (t, J = 6.9 Hz, 2H), 3.24 (t, J = 6.7 Hz, 2H), 2.00 (s, 3H), 1.91(quintet, J = 6.9 Hz, 2H), 1.85 (quintet, J = 6.6 Hz, 2H), 1.27 (br s, 6H).

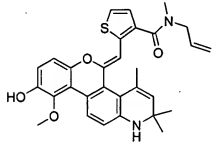
Example 122



(Z)-5-(3'-(2"-dimethoxyethyl)aminocarbonylthiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 138, structure 1 of Scheme I, where R^1 = 2'-(3'-(dimethoxyethylamino)carbonylthiophenyl)

[0282] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(N,N-dimethoxyethyl)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.38 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 5.4 Hz, 1H), 7.01-6.98 (m, 2H), 6.79-6.70 (m, 2H), 5.87 (s, 1H), 5.53 (s, 1H), 3.80-3.53 (m, 7H), 3.41-3.39 (m, 5H), 3.30 (m, 2H, obscured by solvent), 3.13 (s, 3H), 2.00 (s, 3H), 1.29 (br s, 6H).

Example 123

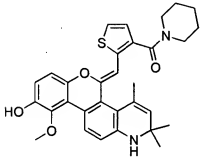


(Z)-5-(2'-(3'-(allylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 139, structure 1 of Scheme I, where R^1 = 2'-(3'-allylmethylaminocarbonyl)thiophenyl)

[0283] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(N-allyl-N-methyl)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, J = 8.8 Hz, 1H), 7.40 (dd, J = 12.4, 5.4 Hz, 1H), 7.01-6.95 (m, 2H), 6.78-6.75 (m, 2H), 5.93 (d, J = 11.7 Hz, 1H), 5.87-5.83 (m, 1.2 H, rotamer), 5.67-5.66 (m, 1.8 H,

rotamer), 5.50 (s, 1H), 5.27-5.08 (m, 2H), 4.10 (m, 0.6H), 3.81 (m, 0.4H), 3.76 (s, 3H), 3.00 (s, 1.2H), 2.81 (s, 1.8 H), 2.02-2.00 (m, 3H), 1.29 (br s, 6H).

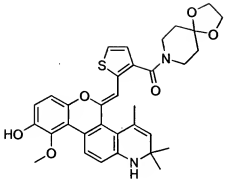
Example 124



(Z)-5-(2'-(3'-(piperidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 140, structure 1 of Scheme I, where R^1 = 2'-(3'-piperidinocarbonyl)thiophenyl)

[0284] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-(piperidine)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, J = 8.8 Hz, 1H), 7.40 (d, J = 5.4 Hz, 1H), 6.97(d, J = 4.9 Hz, 1H), 6.96 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 6.75 (d, J = 8.8 Hz, 1H), 5.93 (s, 1H), 5.50 (d, J = 1.5 Hz, 1H), 3.77 (s, 3H), 3.68-3.65 (m, 2H), 3.30-3.27 (m, 2H, ovlp w/ CD_3OH), 2.03 (d, J = 1.0 Hz, 3H), 1.67-1.63 (m, 4H), 1.47-1.44 (m, 2H), 1.30 (br s, 6H).

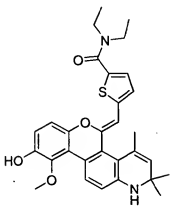
Example 125



(Z)-5-(2'-(3'-piperidinecarbonyl-4"-(1,3-dioxan)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 141, structure 1 of Scheme I, where R^1 = 2'-(3'-piperidinecarbonyl-4"-(1,3-dioxan)carbonyl)thiophenyl)

[0285] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-3-3'-piperidinecarbonyl-4"-(1,3-dioxan)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, J = 8.8 Hz, 1H), 7.41 (d, J = 5.4 Hz, 1H), 7.00 (d, J = 5.4 Hz, 1H), 6.95 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 8.8 Hz, 1H), 6.75 (d, J = 8.8 Hz, 1H), 5.92 (s, 1H), 5.51 (d, J = 1.5 Hz, 1H), 3.97-3.93 (m, 4H), 3.80-3.78 (m, 2H), 3.76 (s, 3H), 3.44-3.41 (m, 2H), 2.01 (d, J = 1.5 Hz, 3H), 1.76-1.73 (m, 2H), 1.60-1.57 (m, 2H), 1.29 (br s, 6H).

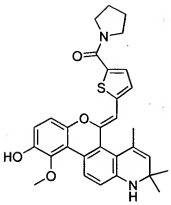
Example 126



(Z)-5-(2'-(5'-(diethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 142, structure 1 of Scheme I, where R^1 = 2'-(5'-diethylaminocarbonyl)thiophenyl)

[0286] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-5-(N,N-diethyl)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, J = 8.3 Hz, 1H), 7.31 (d, J = 3.9 Hz, 1H), 7.01 (d, J = 3.9 Hz, 1H), 6.99 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 8.8 Hz, 1H), 6.75 (d, J = 8.8 Hz, 1H), 5.94 (s, 1H), 5.52 (d, J = 1.5 Hz, 1H), 3.76 (s, 3H), 3.63-3.60 (m, 4H), 2.03 (d, J = 1.5 Hz, 3H), 1.32-1.28 (m, 12 H).

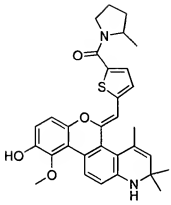
Example 127



(Z)-5-(2'-(5'-(pyrrolidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 143, structure 1 of Scheme I, where R^1 = 2'-(5'-pyrrolidinocarbonyl)thiophenyl)

[0287] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-5-(pyrolidine)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, J = 8.3 Hz, 1H), 7.52 (d, J = 3.9 Hz, 1H), 7.04 (d, J = 3.9 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 8.8 Hz, 1H), 6.75 (d, J = 8.8 Hz, 1H), 5.94 (s, 1H), 5.52 (s, 1H), 3.88-3.85 (m, 2H), 3.76 (s, 3H), 3.65-3.62 (m, 2H), 2.06-1.98 (m, 4H), 2.03 (d, J = 1.5 Hz, 3H), 1.32-1.28 (m, 6H).

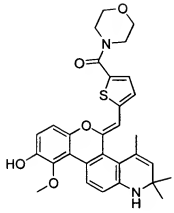
Example 128



(Z)-5-(2'-(5'-(2"-methylpyrrolidinecarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 144, structure 1 of Scheme I, where R^1 = 5'-(2"-methylpyrolidine)carbonylthiophenyl)

[0288] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-5-(2-methylpyrolidine)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (d, J = 8.8 Hz, 1H), 7.49 (d, J = 3.9 Hz, 1H), 7.03-7.01 (m, 2H), 6.77 (d, J = 8.8 Hz, 1H), 6.75 (d, J = 8.8 Hz, 1H), 5.93 (s, 1H), 5.52 (s, 1H), 4.35-4.31 (m, 1H), 3.90-3.85 (m, 2H), 3.77 (s, 3H), 2.16-2.08 (m, 2H), 2.03 (d, J = 1.0 Hz, 3H), 2.0-1.93 (m, 1H), 1.77-1.66 (m, 1H), 1.31-1.27 (m, 9H).

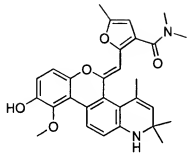
Example 129



(Z)-5-(2'-(5'-morpholinecarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 145, structure 1 of Scheme I, where R^1 = 2'-(5'-morpholinocarbonyl)thiophenyl)

[0289] This compound was prepared according to General Method 2 (Example 65) from 2-methyl-5-(morpholine)thiophenamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.31 (d, J = 8.8 Hz, 1H), 7.27 (d, J = 3.9 Hz, 1H), 6.98 (d, J = 3.9 Hz, 1H), 6.95 (d, J = 8.8 Hz, 1H), 6.73 (d, J = 8.8 Hz, 1H), 6.71 (d, J = 8.8 Hz, 1H), 5.91 (s, 1H), 5.48 (d, J = 1.5 Hz, 1H), 3.78-3.76 (m, 4H), 3.73 (s, 3H), 3.71-3.69 (m, 4H), 1.99 (d, J = 1.0 Hz, 3H), 1.27 (m, 6H).

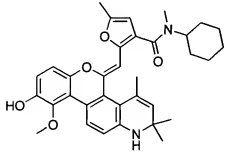
Example 130



(Z)-5-(2'-(3'-dimethylaminocarbonyl-5'-methylfuranylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 146, structure 1 of Scheme I, where R^1 = 2'-(5'-methyl-3'-dimethylaminocarbonyl)furanyl)

[0290] This compound was prepared according to General Method 2 (Example 65) from 2,5-dimethyl-3-(N,N-dimethyl)furanamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.33 (d, J = 8.9 Hz, 1H), 6.78 (d, J = 8.9 Hz, 1H), 6.75 (d, J= 8.5 Hz, 1H), 6.70 (d, J= 8.9 Hz, 1H), 6.16 (d, J = 0.6 Hz, 1H), 5.58 (s, 1H), 5.49 (d, J = 1.5 Hz, 1H), 3.75 (s, 3H), 3.00 (br s, 6H), 2.34 (d, J = 0.9 Hz, 3H), 2.07 (d, J = 1.5 Hz, 3H), 1.28 (br s, 6H).

Example 131



(Z)-5-(2'-(3'-cyclohexylmethylaminocarbonyl-5'-methylfuranylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 147,

structure 1 of Scheme I, where R^1 = 2'-(5'-methyl-3'-(cyclohexylmethylaminocarbonyl)furanyl))

[0291] This compound was prepared according to General Method 2 (Example 65) from 2,5-dimethyl-3-(N-cyclohexyl-N-methyl)furanamide. ^{1}H NMR (500 MHz, CD_3OD) δ 8.32 (d, J = 8.9 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 6.75 (d, J= 8.5 Hz, 1H), 6.71 (d, J= 8.9 Hz, 1H), 6.12 (m, 1H), 5.51 (s, 1H), 5.48 (d, J = 1.2 Hz, 1H), 4.33-4.31 (m, 1H), 3.75 (s, 3H), 2.83 (s, 3H), 2.36 (d, J = 0.9 Hz, 3H), 2.06 (d, J = 1.5 Hz, 3H), 1.77-1.05 (m, 16H).

Example 132

Glucocorticoid Binding Assays

Preparation of GR

[0292] A baculovirus expression plasmid comprising cDNA encoding the human glucocorticoid receptor protein (GR) was prepared using standard techniques. *See e.g.*, E. A. Allegretto et. al. 268 *J. Biol. Chem.*, 26625 (1993); G. Srinivasan and B. Thompson, 4 *Mol. Endo.*, 209 (1990); and D. R. O'Reilly et. al., in "Baculovirus Expression Vectors", D. R. O'Reilly et. al., eds., W. H. Freeman, New York, N. Y., pp. 139-179 (1992). That expression plasmid was co-transfected together with wild type *Autographa californica* multiple nuclear polyhedrosis virus DNA into Spodopter frugiperda-21 (Sf-21) cells to generate recombinant virus comprising GR cDNA. *See e.g.*, O'Reilly, D.R., Miller, L.K., Luckow, V.A., Regulation of expression of a baculovirus ecdysteroid UDP glucosyltransferase gene. "Baculovirus Expression

Vectors." WH Freeman, NY, 139-179 (1992). That recombinant virus comprising GR cDNA was collected.

[0293] A suspension culture of uninfected Sf21 cells was grown to a density of $1.2x10^6$ cells/ml and then infected with the recombinant virus comprising GR cDNA at a multiplicity of infection of 2. Those infected Sf21 cells were incubated for 48 hours and then collected by centrifugation at 1000 x g for 10 minutes at 4°C. The resulting cell pellets were resuspended in lysis buffer (50 mM Potassium Phosphate buffer, pH 7.0, 10 mM Monothioglycerol, 5 mM DTT, 20 mM Sodium Molybdate, 1 mM PMSF, 1 μg/mL aprotinin, and 10 μg/mL leupeptin) and incubated for 15 minutes on ice. Those resuspended cell pellets were homogenized using a Dounce homogenizer and a B pestle. A volume of 2 M KCI was added to the homogenized cell pellets to a final concentration of 0.4 M. The resulting GR lysates were centrifuged at 100,000 x g for 60 min at 4°C and stored for use in binding assays.

Binding Assays

[0294] Binding assay samples were prepared in separate mini-tubes in a 96-well format at 4°C. Each binding assay sample was prepared in a volume of 250 μl of Assay Buffer (10% glycerol, 25 mM sodium phosphate, 10 mM potassium fluoride, 10 mM sodium molybdate, 0.25 mM CHAPS, 2 mM DTT and 1 mM EDTA, (adjusted to pH 7.5)) containing 50 μg of GR lysate; 2-4 nM of [^{3}H]dexamethasone at 84 Ci/mmol; and either a reference compound or a test compound. Test compounds included selective glucocorticoid binding compounds of the present invention. Reference compounds

were unlabeled dexamethasone and prednisone, which have been previously shown to bind to glucocorticoid receptors. Each reference compound and test compound was assayed at varying concentrations, ranging from 0 to 10^{-5} M. Each concentration of each reference compound and each test compound was assayed in triplicate. The assay samples were incubated for 16 hours at 4°C.

[0295] After incubation, 200 µl of 6.25% hydroxylapatite in assay buffer was added to each assay sample to precipitate the protein. The assay samples were then centrifuged and the supernatants were discarded. The resulting pellets were washed twice with assay buffer lacking DTT. Radioctivity in counts per minute (CPM) of each washed pellet was determined by liquid scintillation counter (MicroBeta™, Wallach).

[0296] Specific binding for a particular sample was calculated using the equation:

(Sample CPM) – (Average Non-specific CPM)

Average Non-specific CPM was defined as the amount of radioactivity from samples comprising an excess (i.e. 1000 nM) of unlabeled dexamethasone. IC_{50} values (the concentration of test compound required to decrease specific binding by 50%) were determined using the log-logit (Hill) method. K_i values were determined using the Cheng-Prusoff equation using a previously determined K_d value for dexamethasone:

$$K_i = IC_{50}/(1 + [L]/K_d)$$

[L] = concentration of labeled dexamethasone

K_d = dissociation constant of labeled dexamethasone

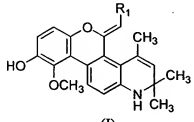
For a discussion of the calculation of K_i, see *e.g.*, Cheng, Y. C. and Prusoff, W. H. *Biochem. Pharmacol.* 22:3099 (1973). K_i values for certain glucocorticoid binding compounds are shown in Table 1.

Table 1. Binding Data

Compound Number	Example	Ki (nM)
11	1	2.7
12	2	0.8
14	4	6
15	5	0.5
18	8	2.5
22	12	4.1
29	19	2.5
37	27	0.9
63	49	1.9
67	53	0.8
75	60	0.8
86	71	1.1
90	75	0.8
97	82	0.9
103	88	1.0
107	92	0.6
111	96	4.3
132	117	1.1
134	118	0.9
138	122	1.4
143	127	1.6
146	130	3.4

WHAT IS CLAIMED IS:

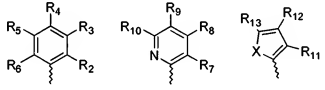
1. A compound of Formula I:



(I)

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, wherein

R_1 is selected from Formula II, III, and IV:



(II) (III) (IV)

wherein:

R_2 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-CONR_{14}R_{15}$, $-OR_{16}$, $-SR_{16}$, $-SO_2NR_{14}R_{15}$, and an optionally substituted aryl,

R_3 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-OR_{16}$, $-SR_{16}$ and an optionally substituted aryl, and

R_4 is selected from hydrogen, F, Cl, Br, CN, $-OR_{16}$, a ring, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_2 and R_3 together form an optionally substituted 5-6 member ring and R_4 is selected from hydrogen, F, Cl, Br, CN, $-OR_{16}$, a ring, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_3 and R_4 together form an optionally substituted 4-6 member ring and R_2 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-CONR_{14}R_{15}$, $-OR_{16}$, $-SR_{16}$, $-SO_2NR_{14}R_{15}$, and an optionally substituted aryl;

R_5 is selected from hydrogen, F, Cl, Br, optionally substituted C_1-C_4 alkyl, and OCH_3;

R_6 is selected from hydrogen and F;

R_7 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-CONR_{14}R_{15}$, and an optionally substituted aryl,

R_8 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -OR_{16}, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, and

R_9 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_7 and R_8 together form an optionally substituted 5-6 member ring and R_9 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, or

R_8 and R_9 together form an optionally substituted 4-6 member ring and R_7 is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl;

R_{10} is selected from hydrogen, F, Cl, CH_3, and OCH_3;

R_{11} is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl,

R_{12} is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4

heteroalkyl, $-OR_{16}$, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, and

R_{13} is selected from hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_{11} and R_{12} together form an optionally substituted 5-6 member ring and R_{13} is selected from hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_{12} and R_{13} together form an optionally substituted 4-6 member ring and R_{11}, is selected from hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, $-CONR_{14}R_{15}$, and an optionally substituted aryl;

R_{14} and R_{15} are each independently selected from hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl, or

R_{14} and R_{15} together form an optionally substituted 4-7 member ring;

R_{16} is selected from hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_1-C_4 heteroalkyl, and an optionally substituted aryl;

X is selected from O, S, and NR_{17};

R_{17} is selected from hydrogen and an optionally substituted C_1-C_4 alkyl; and

wherein

at least one position selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen;

at least one position selected from R_7, R_8, R_9, and R_{10} is not hydrogen;

if R_4 is F, then at least one position selected from R_2, R_3, R_5 and R_6 is not hydrogen;

if R_3 is F, then at least one position selected from R_2, R_4, R_5, and R_6 is not hydrogen; and

if any two positions selected from R_2, R_3, R_4, R_5, and R_6 are both F, then at least one of the other three positions selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen.

2. The compound of claim 1 wherein R_2 is an optionally substituted aryl wherein the optionally substituted aryl is a phenyl that is optionally substituted with a substituent selected from hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

3. The compound of claim 1 wherein R_8 is an optionally substituted aryl wherein the optionally substituted aryl is a phenyl that is optionally substituted with a substituent selected from hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

4. The compound of claim 1 wherein R_{11} is an optionally substituted aryl wherein the optionally substituted aryl is a phenyl that is optionally substituted with a

substituent selected from hydrogen, a halogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, and an optionally substituted C_1-C_4 heteroalkyl.

5. The compound of claim 1 selected from:

(a) (Z)-5-(3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',5'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-trifluoromehoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-trifluoromehoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-trifluorothiomethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-fluoro-3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-fluoro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',4'-dichlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-chloro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-di(trifluoromethy)lbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-fluoro-5'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',4',5'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-ethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-fluoro-2'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-6'-fluorobenzylidene)1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-isopropylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-fluoro-4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(6'-methyl-pyridinylmethylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-methyl-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-benzyloxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-methy-4'-fluorolbenzylidene)-1,2-dihydro-9-(3-methyl-4-fluorobenzoyloxy)-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-cyclohexylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-chloro-4'-trifluoromethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',6'-difluoro-3'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-3',6'-difluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-methyl-3'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-fluoro-4'-chlorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3'-difluoro-4'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3',5',6'-tetrafluoro-4'-trifluoromethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-dimethylaminocarbonyfuranylmethylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-vinylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-Chloro-6'-fluoro-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-trifluoromethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-trifluorothiobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',4'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-chloro-2'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-(4"-methylbenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-di-tert-butylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2",2"-difluoroethoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',5'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3"-thiophene)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-diethylaminocarbonylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4",4",4"-trifluorobutoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2",4"-difluorophenyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3"-pyridyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3"-benzenecarbaldehyde)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',4'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(diethylamino)carbonyl-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(diethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(methylbenzylamino)carbonyl-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(di-methylamino)carbonyl-5'-bromo-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2"-fluoroethoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2",2",3",3"-tetrafluoropropoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-fluorobenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2"-fluorobenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(pyrolidinecarbonylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(pyrolidinecarbonyl-5'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(di-methylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(pyrolidinecarbonyl-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(pyrolidinecarbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-fluorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(morpholinecarbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-fluoro-benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-dimethylcarbonyl-3'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(4"-methylpiperazine)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-methyl-3'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3',5'-di-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(piperidineamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-dimethylaminosulphonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(ethylmethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(cyclohexylmethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-cyanobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3',5',6'-tetrafluoro-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-hydroxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(piperidinesulphonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-napthylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-methyl-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2-cyclohexyl-4-methyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',5'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2-cyclohexyl-4-methyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2',3'-ethylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4'-hydroxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-cyano-3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-chloro-2'-cyanobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-bromo-2'-cyano-benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-chloro-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-chloro-3',4'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-cyano-3'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(5'-methyl-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-cyano-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(4',5'-difluoro-Benzo-1,3-dioxan-methylidiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3",5"-dichlophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-methoxy)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3",4"-dichlorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-methyl)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(4"-chloro)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(3"-trifluoromethoxy)phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4- f]quinoline;

(Z)-5-(2'-(3'-(dimethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(ethylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(morpholinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-cyclohexylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(pyrrolidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(3'-(2"-dimethoxyethyl)aminocarbonylthiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(allylmethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-(piperidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-piperidinecarbonyl-4"-(1,3-dioxan)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(5'-(diethylaminocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(5'-(pyrrolidinocarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(5'-(2"-methylpyrrolidinecarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(5'-morpholinecarbonyl)thiophenylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-dimethylaminocarbonyl-5'-methylfuranylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline;

(Z)-5-(2'-(3'-cyclohexylmethylaminocarbonyl-5'-methylfuranylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline; and

(b) a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

6. The compound of claim 1, wherein the compound is a selective glucocorticoid receptor modulator.

7. The selective glucocorticoid receptor modulator compound of claim 6 that is a glucocorticoid receptor agonist.

8. The selective glucocorticoid receptor modulator compound of claim 6 that is a glucocorticoid receptor antagonist.

9. The selective glucocorticoid receptor modulator compound of claim 6 that is a that is a glucocorticoid receptor partial agonist.

10. The selective glucocorticoid receptor modulator compound of claim 6 that is a tissue-specific modulator.

11. A selective glucocorticoid binding compound of claim 1.

12. A method for modulating an activity of a glucocorticoid receptor comprising contacting a glucocorticoid receptor with at least one compound of claim 1.

13. The method of claim 12 wherein the glucocorticoid receptor is in a cell.

14. A method for identifying a compound that is capable of modulating an activity of a glucocorticoid receptor, comprising:

contacting a cell expressing a glucocorticoid receptor with a compound of the present invention; and

monitoring an effect of the compound upon the cell.

15. A method for treating a patient comprising administering to the patient a compound of claim 1.

16. The method of claim 15 wherein the patient suffers from a condition selected from inflammation, acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, granulomatous disease, immune proliferation/apotosis, HPA axis suppression and regulation, hypercortisolemia, modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hyperglycemia, cerebral edema, thrombocytopenia, Little's syndrome, Addison's disease, cystic fibrosis, myasthenia gravis, autoimmune hemolytic anemia, uveitis, pemphigus vulgaris, multiple sclerosis, nasal polyps,

sepsis, infections, type II diabetes, obesity, metabolic syndrome, depression, schizophrenia, mood disorders, Cushing's syndrome, anxiety, sleep disorders, memory and learning enhancement, and glucocorticoid-induced glaucoma.

17. A pharmaceutical agent comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

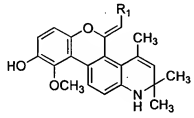
18. A pharmaceutical agent of claim 17 for use in treating a condition selected from inflammation, acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, granulomatous disease, immune proliferation/apotosis, HPA axis suppression and regulation, hypercortisolemia, modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hyperglycemia, cerebral edema, thrombocytopenia, Little's syndrome, Addison's disease, cystic fibrosis, myasthenia gravis, autoimmune hemolytic anemia, uveitis, pemphigus vulgaris, multiple sclerosis, nasal polyps, sepsis, infections, type II diabetes, obesity, metabolic syndrome, depression, schizophrenia, mood disorders, Cushing's syndrome, anxiety, sleep disorders, memory and learning enhancement, glucocorticoid-induced glaucoma.

19. The pharmaceutical agent of claim 18 for use in treating a condition of inflammation wherein the condition of inflammation is selected from rheumatoid arthritis, asthma, lupus, osteoarthritis, rhinosinusitis, inflammatory bowel disease, polyarteritis nodosa, Wegener's granulomatosis, giant cell arteritis, allergic rhinitis,

urticaria, hereditary angioedema, chronic obstructive pulmonary disease, tendonitis, bursitis, autoimmune chronic active hepatitis, and cirrhosis.

Abstract of the Disclosure

[0297] Disclosed herein are compounds of Formula I:



(I)

and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof. Certain of such compounds are selective glucocorticoid receptor modulators and/or selective glucocorticoid binding agents. Also disclosed are methods of making and using such compounds, including, but not limited to, using such compounds for treating various conditions.